THE JOURNAL
of the American Medical Association
Published Under the Auspices of the Board of Trustees

Acc. No.
Date
Price

VOL. 162, NO. 9
CHICAGO, ILLINOIS
OCTOBER 27, 1956

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EVALUATION OF END-RESULTS OF ACUTE ANTERIOR POLIOMYELITIS

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• *Poliomyelitis does not actually have a chronic phase, when considered in terms of static functional capacity and reaction to stress. The end-results of this disease can be evaluated any time after the period of rapid recovery has taken place and the patient is old enough chronologically, and in duration of illness, to have had all the necessary treatment. This evaluation, which must be on an individual basis, must include not only the degree of physical independence but also the patient's mental adjustment to his residual physical handicap. Evaluation can only be carried out by the physician who, considering all the many factors determining recovery, judges without bias.*

The desired end-result in poliomyelitis is achieved when (1) the patient has obtained or regained the highest possible degree of safe physical independence within the limitations imposed by factors over which there is no human control and (2) the patient has made an intelligent adjustment to his residual handicap. The degree to which this dual goal has been reached can be evaluated only by the physician who, considering all factors that molded the end-result, judges without bias. The purpose of this paper is to discuss factors that determine the end-results, regardless of treatment, and some of the more important criteria by which the effectiveness of treatment may be determined.

We must first decide when we are justified to judge end-results. Experience has taught us that poliomyelitis actually has no chronic phase, if we speak in terms of static functional capacity and reaction to stress. Poliomyelitis is forever to those who have significant after-effects, and the deforming possibilities of age and activity are with them as long as they live. We can only state arbitrarily that an evaluation of end-results may be made at any time after the phase of rapid recovery has taken place and the patient is old enough chronologically, and in duration of illness, to have had all necessary treatment.

Factors Determining Recovery

No end-results can possibly be graded as good, bad, or indifferent, particularly when judging the effectiveness of treatment, unless factors that modify recovery, regardless of treatment, are also considered.

Site and Extent of Central Nervous System Involvement.—Each muscle has what might be called a normal complement of anterior horn cells arranged in fairly well-defined columns within the anterior horn of the spinal cord. Some muscles are innervated by short columns of cells extending over little more than one segment of the spinal cord. Other muscles may have long columns extending over five or even six segments. Therefore, a relatively mild destruction of anterior horn cells extending over one or two levels of the spinal cord might completely denervate muscles with limited normal innervation and largely spare those with multiple levels of innervation. While each muscle is important in some phase of functional activity, certainly it must be admitted that all muscles are not of the same importance. Lesions at the cervical level are more apt to cause greater loss of functional capacity than lesions of a comparable size at thoracic or lumbar levels. Therefore, the site and extent of the irreversible damage to the central nervous system must determine to a most significant degree the eventual recovery of physical activity, regardless of treatment.

Availability of Adequate Medical Care.—It must be accepted that adequate medical care will minimize the after-effects of this disease. Adequate care must be adequate total care. The finest convalescent care cannot overcome the faults of management of care in the acute stage nor wholely protect the patient from inadequate or faulty care in the chronic stage. Despite the most conscientious effort, recovery may be limited because of limited personal and community resources. Epidemics tax the resources of even the best-prepared community, and only minimal facilities are available throughout the country for those persons with severe involvement.

Medical Condition of Patient.—If the medical condition of the patient prohibits the use of care necessary to optimum recovery of his neuromuscular system, weaknesses will persist and deformities will develop that could otherwise have been prevented. A patient

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Read before the Section on Physical Medicine at the 105th Annual Meeting of the American Medical Association, Chicago, June 12, 1956.

confined to a respirator simply cannot have all the necessary treatment for his skeletal muscular involvement that would otherwise be possible. At any time during the patient's life medical problems entirely apart from the after-effects of poliomyelitis might seriously interfere with his continued recovery or his maintenance of muscular strength and skeletal alignment.

Age of Patient at Onset of Acute Anterior Poliomyelitis.—From a structural standpoint, the infant that develops significant muscular weakness is a far greater problem than the adult with comparable weakness. Despite the finest treatment, such an infant must develop certain changes in structural alignment as he grows taller and increases in both weight and activity. Growing bone demands balanced musculature for its alignment, and, regardless of the best supportive apparatus available, some degree of deformity must result. The infant and youngster cannot be expected to appreciate the necessity for restriction of activity and the avoidance of abnormal patterns of movement. They therefore tend to develop marked muscle imbalance, despite the most conscientious supervision. Their response to specific muscle reeducation is limited for the same reason. Psychologically, each age has its own problems. The teen-ager is particularly difficult to cope with because of his interest in his physical self at this age. His adjustment to this loss of physical capacity is extremely difficult. The infant, never knowing normal physical capacity, has a somewhat easier time accepting his limitations. The young adult, man or woman, particularly when married and just starting out on a career, finds physical handicap extremely difficult to accept and is plagued by the fear of insecurity and inadequacy. Structural growth, nancial insecurity, and the loss of sense of personal rth may be far greater problems influencing the nd-results than the actual physical handicap caused by muscle weakness alone.

Personality of Patient, His Family, and His Community.—I think it is only fair to say that, if a patient with significant and lasting muscle weakness makes a good physical and psychological adjustment to his handicap, a great share of the credit must be given to the patient, his family, and his community. This statement is not meant to detract from the credit due the physician but rather to emphasize the importance of the attitude and responsibility of the patient and all those about him who mold the end-results, from a physical standpoint as well as socially, vocationally, and economically. Without their complete cooperation, the physician alone is incapable of maximum results, regardless of his knowledge and skill. This is particularly true of the young child who must be kept under the disciplines of restricted activity and tedious home routines for long years after the period of rapid recovery has taken place. It is hard for families to understand that this monotonous program is designed simply to keep the child growing as straight as possible until structural security is assured by mature bone growth or until necessary orthopedic surgery can be carried out at the proper age. Patients cannot be hospitalized endlessly, nor can the doctor and therapist in an outpatient department be responsible for total care. The patient must be returned to his home in a reasonable period of time, and he and his family must accept most of the responsibility of continued care.

Criteria for Judging End-Results

It should be apparent to each of us that we cannot judge the effectiveness of treatments by setting forth a list of functional activities and arbitrarily deciding that a good result means the accomplishment of a high percentage of these activities and a poor result the accomplishment of but a few. A good result, or a poor result, depends entirely on what was done with what was left to work with, not in terms of the percentage of normal capacity regained but in terms of the maximum response such involvement will allow under what might be considered ideal circumstances. Many results that might be considered poor when compared to the average response might actually be excellent if we consider the tremendous odds against which these particular patients were fighting. On the other hand, results quite acceptable to average patients should be considered poor if the patients evaluated have had every advantage and have made little use of them.

The success or failure of the care of the after-effects of poliomyelitis might well be determined by the answer to one basic question: Has the patient, through treatment, obtained maximum safe and practical functional capacity possible within the limits imposed by the factors that determine end-results, regardless of treatment? This question fairly indicates the objectives of treatment and, therefore, the physician's goal in his care of his patient. The degree to which this goal has been achieved can be determined only after the consideration of the following six points by which the physician should analyze his results.

Pattern of Residual Weakness.—The after-effects of poliomyelitis show characteristic patterns of residual weakness. Good treatment can favorably modify these patterns, but only to a moderate degree. Poor treatment not only exaggerates these patterns but actually causes patterns that can be identified as due to faulty treatment. This point is not easy to discuss, because we are immediately faced with the knowledge that we are actually unable to determine the precise damage done by the virus and must accept the fact that any distribution of anterior horn cells could be involved. Few diseases permit us to excuse our mistakes so easily. However, long experience with this disease has shown us that identical combinations of specific muscular weaknesses occur so frequently as to be expected, and deviations from these combinations must be viewed with suspicion of faulty care. Clinical and pathological studies by many investigators have repeatedly shown the striking combinations of muscle weaknesses that appear to be characteristic of the after-effects of poliomyelitis. This was noted as early as 1908 by Lovett and Lucas[1] and was well discussed in a more recent paper in 1955 by Sharrard.[2] Actually, little experience is necessary to state that, if a bizarre pattern exists or if isolated severe muscle weakness is found in a bodily segment otherwise not involved, we have good reason to believe that the damage was done by extrinsic factors of overwork or disuse rather than neuron distruction due to virus invasion. Isolated weakness in the serratus and in the triceps surae and muscle imbalance in the abdominal muscles occur so frequently from these causes that they need no further discussion. Other patterns are far more difficult to detect and require a great deal of experience on the part of the evaluating physician. In many instances only repeated observation of the habit patterns of movement in individual patients will bring out the true reason for faulty recovery.

Musculoskeletal Deformities.—Except for atrophy of muscle, which must follow permanent denervation, and retardation of skeletal growth, the cause of which is not completely understood, all other deformities of the musculoskeletal system are at least theoretically preventable by proper care. However, some degree of deformity must develop in bodily segments if residual weakness exists and necessary activity brings about abnormal stress on these bodily segments. Despite adequate mobilization, muscle reeducation, graded activity, and externally applied supports, some degree of structural deformity will take place in the growing child and even in the adult if muscle weakness persists. The physician, however, must accept the responsibility of minimizing these deformities. Through accepted methods of care the physician must show proof that he has anticipated the development of significant deformities by evaluating the causes of these deformities and doing everything possible to prevent their development by properly timed conservative and surgical methods. Since the existence of deformities definitely limits the goal of maximum possible functional recovery and the patient's acceptance of his physical handicap, the evaluation must indicate the degree to which the deformities have been anticipated and corrected. Because it is impossible to prevent or correct all deformity, the evaluation must show the extent to which the physician has recognized these deformities and made an effort to overcome them. The physician who attempts to evaluate these end-results must obviously know the pathogenesis of deformity and the accepted methods for prevention or correction.

Apparatus.—The use of various types of orthotic devices has now become an accepted part of both convalescent and chronic-phase care. Certainly the effectiveness of any method of treatment must never be evaluated solely in terms of the amount of apparatus used. Great advances have been made in the design, weight, and fitting of supportive and assistive apparatus, and this apparatus may be essential to the achievement of maximum safe and practical functional capacity and the patient's intelligent acceptance of his physical handicap. It is just as great a fault not to use an apparatus that is necessary as it is to apply an apparatus that should not have been used at all.

Orthopedic Surgery.—It should be pointed out that there is no evidence to show that ideal treatment decreases the number of necessary and effective orthopedic surgical procedures. Ideal treatment, on the other hand, should have eliminated the need for unnecessary surgical procedures and, at the same time, should have assured maximum results from those procedures that were necessary. The effectiveness of any form of treatment should never be based on the number of orthopedic surgical procedures that were used. Such surgery is frequently necessary to increase functional capacity and structural security. Like the proper use of necessary apparatus, necessary orthopedic surgery should also be considered a part of good over-all care. If orthopedic surgery was done, an end-result evaluation must determine whether the surgery was really necessary and whether it actually accomplished the purpose for which it was intended. Orthopedic surgery cannot be expected to cure all the ills of muscle weakness, muscle imbalance, and structural deformity, but, on the other hand, there must be every evidence that surgery was properly timed and the procedures used were well thought out and executed. Like all other forms of treatment, surgery can cause more harm than good if improperly applied.

Evidence of Specific Functional Training.—The person with severe involvement cannot achieve effective functional capacity without skilled training. The degree to which he develops both safety and endurance for the necessary physical activities must reflect the training that he has had. The finest surgical procedures, or the finest apparatus, can be of little value unless the patient is taught how to profit from the results of such procedures or apparatus. The patterns of physical activity not only must be safe and practical but also must be acceptable to both the patient and the individuals with whom he must live. Only the physician well versed in the possibilities of developing functional capacity in the person with severe involvement can possibly evaluate this component of the end-result.

Attitude of Patient Toward His Handicap.—The last, but in many ways the most important, point to consider is the patient's personal reaction to his handicap. The medical-care program, to be considered really adequate, must accept the responsibility of assisting the patient to make an intelligent adjustment to his ultimate handicap. Even minimal physical handicap requires some degree of adjustment on the part of the patient. To adjust adequately, the patient must be sure in his own mind that he has all the treatment necessary. He must know the full extent of his limitations; he must be able to interpret his own limitations not only in terms of the normal individual but in relationship to those with more severe and less severe physical handicap. The extent to which the patient has adjusted vocationally, socially, and recreationally must be the points by which he is judged in this phase of the end-result of his disease.

Summary and Conclusions

An evaluation of the end-results of poliomyelitis must be made on the basis of individual patients. An adequate end-result may be said to have been achieved when the patient has obtained or regained the highest possible degree of safe physical independence within the limits imposed by factors over which there is no control and, in addition, when the patient has made an intelligent adjustment to his residual physical handicap.

Since we are unable to determine precisely the actual damage to the nervous system by the invasion of the virus and its uncontrollable after-effects, we find it easy to excuse our bad results on the grounds of unpreventable pathology.

The multiple variations of involvement make a listing of functional achievements a formidable, if not impossible, task. If we add to these variations of muscular involvement and their skeletal after-effects the even greater numbers of variations in patients' age, background, personality, and environment, the listing of expected achievement becomes truly impossible. The degree to which both the patient himself and his medical supervisor have taken advantage of the full possibilities of recovery can be judged only by the experienced but unbiased physician after full consideration of all factors that determine the ultimate recovery.

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PREVENTION OF PSYCHIATRIC ILLNESSES

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• *Epidemiological studies show that prevention, not primarily treatment, appears to be the logical long-term solution to the mental illnesses. Past investigations reveal this particular group of diseases may fall into three etiological classifications: organic brain damage, individual stress, and what might be called group stress resulting from cultural patterns.*

The prevention of somatic pathology is fairly well understood, especially where there is a single causative factor. The detrimental effects of individual stress might be obviated through much of our present-day knowledge of personality formation. It is in the area where social customs seem to be the dominating determinant of psychiatric illness, however, that new research is needed.

The major successes in the prevention of disease have been in dealing with that group in which there is one outstanding and overwhelming cause for the disease.[1] For the most part, these successes have been in the prevention of diseases of bacteriological or viral origin in which the essential etiological factor is an invasion of the body by an external agent. We have had much less success with illnesses that arise within the body itself, such as arthritis, cancer, diabetes, and arteriosclerosis. In these, we probably deal not with a single overwhelming cause but with a series of causes that must in some way act together to produce disease.

It is true that these two general groups of illnesses cannot be entirely separated, and that more and more we begin to recognize, under the leadership particularly of Dubose,[2] that even those diseases fundamentally related to the invasion from the outside depend upon the condition of the body invaded. Dubose, by means of ingenious experiments, is bringing back into focus the common folk ideas that drafts cause colds; that, in other words, overexposure predisposes the body to external invasion. The relationship between recent severe physical activity and the appearance of paralysis in poliomyelitis is another case in point. It is well recognized, particularly in tuberculosis, that psychological stresses in the family, at work, and elsewhere seem frequently to be related to the appearance of actual illness.[3]

In the mental illnesses, the concept of the single important cause of disease is more difficult to apply. Indeed, one psychiatrist, Dr. Robert Felix, has made the statement—not entirely seriously—that schizophrenia acts like tuberculosis in which the bacillus is absent. He is saying that it is at least possible that schizophrenia is a reaction to complicated, difficult, stressful life situations; that for this disease it is these life situations themselves that are the cause; and that no adjunctive bacterium needs to be present to give the resulting illness a particular charcter.

The issues of the prevention of psychiatric illnesses are extremely complex. One reason for this complexity is that we tend to think of psychiatric illness as a unit, instead of considering the multiple and relatively independent illnesses that are included in that unit. There are some psychiatric illnesses in which the etiology is as clear as it is in the physical diseases in which an invader of external origin is of overwhelming importance. For these psychiatric illnesses, prevention is as easy to consider as it is in connection with typhoid or pneumonia. There are other illnesses, however—and these are the ones that give the greatest difficulty—in which there is no single destructive invasive cause.

Another problem that makes it difficult to think about the prevention of psychiatric illness is the extraordinary fluidity of the field. In the last 30 years, psychiatry has seen the introduction of many new types of treatment. It appears fair to say that research and theory have not entirely been able to keep up with empirical advances in the field. We have gone through a period of innovations in shock therapy using insulin, pentylenetetrazol (Metrazol), and electricity; yet in none of these has the function of the treatment in controlling psychiatric illnesses been completely explained. We have seen the introduction of brain surgery for the relief of psychiatric syndromes, but we are still without an adequate and complete explanation of the effectiveness of these operations in some cases. More recently, there has been the introduction of drugs such as lysergic acid and its derivatives and some of the hormones and hormone-like substances, which, under certain circumstances, induce psychotic behavior in human beings. In addition, the extremely rapid introduction and widespread use of the behavior-regulating drugs, chlorpromazine and the Rauwolfia derivatives, have again produced a therapeutic agent the mechanisms of whose action are not clearly understood. Certainly the relationship of these drugs

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Read before the Section on Preventive and Industrial Medicine and Public Health at the 105th Annual Meeting of the American Medical Association, Chicago, June 14, 1956.

to, for example, schizophrenia, is far different from the specific relationship of insulin to diabetes mellitus. Yet, it is likely that the length of time it has taken to understand carbohydrate metabolism and the effectiveness of insulin in its regulation resembles the length of the time it will take for psychiatric study and research to solve the problem of the effect of the behavior-regulating drugs on the function of the brain.

In this year of the 100th anniversary of Freud's birth, it is well to recognize also that it has been but 40 or 50 years since the introduction of his concepts of the psychogenesis of the mental illnesses, and that there have been, in that time, numerous corrections and reformulations of his ideas. It is safe to say at the present time that psychiatric research and theory have not, by any means, caught up with the numerous hypotheses he postulated. In other words, psychiatry remains without a completely sound theory of either the causation of the psychogenic mental illnesses or the effect of empirical treatment.

Findings of Epidemiological Research

There is another aspect of rapid change in the psychiatric field to be accounted for in any discussion of the prevention of psychiatric illnesses. This relates to the findings of epidemiological research. The problem appears in such overwhelming proportions that the need for its control has become perhaps the major issue in the public health programs of the future. Some of these findings are very trite; for example, that half of the hospital beds in our nation are occupied by patients with psychiatric illnesses, most of them chronic. In addition, there are the data concerning the prevalence of psychiatric illness not requiring hospitalization. The two best current studies of this field appear to indicate that psychiatric symptoms severe enough to require treatment may be present in as much as 30% of the population.[4] Older studies about the prevalence of psychiatric complaints in the practices of physicians are so well known that their findings need not be repeated here.[5]

Epidemiological studies have, however, gone beyond merely pointing with alarm to the large number of cases existing. There are studies that indicate that mental deficiency, epilepsy, cerebral palsy, and certain other illnesses are probably directly related to various obstetric complications, particularly hypertension of pregnancy, eclapsia, and bleeding in the third trimester.[6] It appears clear that the prevention of these more or less static conditions that are due to inadequate development, or to direct damage to central nervous system tissue, can be prevented to a considerable degree if the problems of obstetric care can be solved.

Epidemiological studies have gone further than this and have demonstrated that there are certain groups in the population that must be the subject of particular concentration if mental illnesses are to be prevented. It is quite clear that the underprivileged group in the population—underprivileged economically and educationally, probably nutritionally, and certainly in housing opportunities—produces far more of the mental illnesses of all kinds than one would expect if these illnesses were evenly distributed in the total population.[7] This leads to the consideration of cultural factors that in some way reduce the threshold for the appearance of mental illnesses in these underprivileged groups.

Thus, in any approach to the problem of the prevention of the psychiatric illnesses, it must be recognized that this group of diseases includes syndromes in which there is an overwhelming cause, for example, encephalitis or brain trauma; illnesses in which there is a nutritional or metabolic disorder, for example, macrocytic anemia and, in a sense, also arteriosclerosis; and illnesses that are exclusively due to chronic reactions to debilitating life circumstances of a personal, as well as of a broader cultural, type.

Opportunities for Prevention

With present knowledge and the rapid extension of theory and laboratory knowledge in this field, what are the present opportunities for prevention? The easiest group of illnesses to deal with is that due to a single cause arising outside the individual. There is nothing new in the concept of the prevention of paresis by the prevention or early treatment of syphilis. If the basic disease, syphilis, is controlled, paresis cannot occur. If there is no tuberculosis, there can be no tuberculoma of the brain, with a consequent behavior disorder, nor tuberculous meningitis, with residua due to destruction of the brain cortex. If there is no traumatic destruction of brain tissue, there can be no post-traumatic psychosis. For the most part, the prevention of this kind of mental illness does not lie in the hands of psychiatrists. It lies directly at the door of public health and, with a few notable exceptions, public health has handled this problem well.

Individual Stress.—The psychiatrist, however, is deeply concerned with the alleviation of the individual and cultural stresses on the person that lower the threshold for the appearance of illness. It must be admitted that in this area the case rests almost entirely at the present time on hypothesis. There is a growing literature on experiments in animals showing that long-continued severe stress upon the individual will cause overgrowth of certain hormone-producing glands. These data make more understandable the precise mechanisms by which the threshold of response, with disease or symptom-reactions, is lowered by long-continued stress. It cannot be said, however, that this mechanism is entirely understood at the present time and, as has been pointed out already, there are undoubtedly many such mechanisms that would have to be considered in order to understand all of the psychiatric illnesses that can be distinguished, even within this field of psychogenic illnesses.

The problem of prevention then becomes the avoidance of stress that is so great that it exceeds the capacity of the individual to deal with it and eventually lowers his ability to withstand the appearance of psychiatric illness.[8] At the level of individual stress, it is believed that the best work can be done during the period of rapid structuralization of the personality that takes place in childhood. The newer experiments on the effect of isolation of infants and very young children, which indicate that inadequate stimulation of innate capacities can lead to the atrophy of these capacities, tend to point to the importance of early childhood as an area for preventive work.[9] Thus, it would appear that every child, every infant, ought to have a person near to stimulate him to use all of the capacities he has available—capacities to move, capacities to learn, capacities to react emotionally, capacities to love; all these must be exercised lest they atrophy and thus become no longer available for later development. This avoidance of understimulation, both intellectually and emotionally, is not, however, confined to early infancy. It can also be shown that the elderly who are denied social intercourse and stimulation tend to lapse into psychotic disorders more often than those living in better and more stimulating social circumstances.[10] In short-term experiments, it can be shown that healthy young adults, if drastically denied any outside stimulation, will quickly react with psychiatric symptoms such as hallucinations and delusions.[11]

There appear to be many opportunities for the prevention of unnecessary stress on the individual in the parent-child relationship. The study of child development shows that certain types of behavior are normal in children but are also considered bothersome, unhealthy, and embarrassing by many in our culture. For example, many mothers are excruciatingly embarrassed when their children of 3 throw temper tantrums at a supermarket, and yet it can be safely predicted that 80% of healthy children in most United States environments will throw temper tantrums. In such a circumstance, the acute embarrassment seems rather futile and might well be replaced with an understanding that during the period of negativism children do have temper tantrums, and that this is a step in the development of mature emotional reactions. In our culture, particularly in middle-class culture, it is well known that a high percentage of children between the ages of 2 and 5 will show a great deal of food refusal. Yet there are many mothers and fathers who go through the tortures of the damned trying to get their children to eat food in the amounts they think are necessary during this period. When a reaction such as food refusal is common, it would appear useless to expend so much anxiety about it. Some knowledge on the parents' part not only of the fact that food refusal is all but universal in children during this period but also of the fact that there is probably reduced need for food during this period of slow growth would certainly prevent a great deal of unnecessary anxiety, irritation, and anger.

In adolescence, there is the accelerated maturation of the female as compared to the male, so that the 13-year-old or 14-year-old female seeks her companionship from 16-year-old or 17-year-old males. Many parents worry because they fear their daughters are going to be exploited sexually by these "older men," whereas the girl is actually seeking companionship with people of her own developmental rather than her chronological age. Many junior high schools and high schools are deeply concerned by this problem, which includes such questions as, for example, who shall be invited to school dances, since the taller girls will not dance with the shorter boys of their own age. Such problems interfere with a mutually appreciative relationship between parent and child and generally represent useless anxiety based on ignorance of child development, anxiety that knowledge can relieve. To be sure, knowledge itself is frequently ineffective; it must be transmitted in a setting that allows attitudes to mature and change at the same time that the knowledge is being given.

Cultural Stress.—In our culture many adults face common problems that are also more than necessarily stressful in the absence of knowledge. For example, most women face childbirth with great stress. Yet it is well recognized that the stress of childbirth is much less if the process is understood and prepared for than if the experience comes with no understanding. Although it cannot thus far be statistically demonstrated, it is believed that proper preparation for marriage tends to reduce postmarital adjustment problems. It has been shown that relatively brief and unsophisticated discussion of such problems as fear, reaction to authority, and homesickness can reduce the incidence of psychiatric illnesses and behavior disorders in inductees entering military service. It has not yet been demonstrated but it is widely believed that preparation for retirement, and anticipation and preparation for the use of leisure time coming after retirement, might well prevent the excessive rates of suicides in older men and, perhaps, also the appearance of senile psychosis in people whose retirement has left them with a vacuum in their lives.[8]

The psychiatrist is in a difficult position when he addresses himself to the findings of epidemiology that indicate the high concentration of illnesses in the underprivileged social classes. Here one rapidly approaches the problems of welfare, housing, and public recreation, which are so heavily loaded politically that the physician hesitates to take a stand. The full implications of the World Health Organization definition of health have not yet been worked out. This statement defines health not only as the absence of disease but as physical, mental, and social well-being. In general, medicine is not yet prepared, theoretically or empirically, to deal with these broad, economically tinged problems of social health, nor can one foresee what developments will come as this far-seeing definition begins to affect medical practices more and more. There are certainly germs of ideas for the prevention of psychiatric illnesses coming from these studies. It remains extremely difficult as we presently see "through a glass, darkly" the means of bringing these germs into flowering programs for the prevention of illness.

There is, however, one cultural fact that must indeed give pause. This is the recurring finding that half of the medical and welfare services available to all the community are expended upon a relatively small segment of the population, the now famous "6%."[12] The whole concept of the clustering of diseases of all kinds—psychiatric, physical, and social—in a relatively small group of the population must be considered, for, if some rehabilitation program could be made to succeed for this 6% of the population, we could, in all likelihood, prevent 50% of our social, psychiatric, and physical illnesses. The methods of doing this have not yet been formulated, but they represent one of the most inviting areas for research.

Summary

In considering the prevention of psychiatric illnesses, it must constantly be kept in mind that we are not dealing with a single scheme of prevention but rather with a multitude of illnesses, many of which have specific preventions applicable to them alone. I refer primarily to the mental illnesses secondary to the destruction of central nervous system tissue. On the other hand, there is a large group of psychiatric illnesses that appear to be related to chronic, severe stresses—individual stresses or cultural stresses. It may be possible to reduce individual stresses through education and changing attitudes, particularly in the area of child-parent relationships. There is an approach, not yet fully understood, for the prevention of psychiatric illnesses through the relief of broad cultural stresses playing upon large groups of individuals.

Presently, we are able to work quite exactly in the prevention of brain damage. The relationship between cause and effect is clear and predictable. In the area of the prevention of excessive stress upon the individual, the data are much less exact and the multiple factors have as yet defied final and clear-cut predictability from hypothesized cause to realized illness. It is these two areas, however, where most effective work with present knowledge can be done. We must address ourselves to the future for methods that can be effective in dealing with the third area, the relief of stress playing upon particular groups within the culture—the stresses themselves having their origin, to some extent at least, within the practices of the culture.

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EMOTIONAL FACTORS IN GASTROINTESTINAL DISORDERS

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• *Not only functional disorders but also gross organic lesions in the gastrointestinal tract can be caused by emotional stimuli The functional disorders include nervous vomiting, anorexia nervosa, nervous diarrhea, constipation, and irritable colon The disturbances of function may lead to the organic lesions, of which good examples are peptic ulcer and chronic ulcerative colitis A case of the latter is described to exemplify the striking improvement that sometimes follows removal of the patient from a difficult environment. Such problem cases require study and treatment of the total organism and may necessitate consultation between social service department, psychiatrist, and internist.*

I have chosen this opportunity to reemphasize the emotional factors in gastrointestinal disorders This is not a new subject, nor is it a recent concept. Although little evidence can be found in communications prior to this century, it has been well presented in many writings, usually by psychiatrists or strongly oriented psychosomatic internists We who are interested in internal medicine, and especially those of us whose interests lean toward the field of gastrointestinal disease, are grateful to the psychiatrists for their continuous emphasis on the great role that the psyche plays in gastrointestinal disorders. We are often confused by the arguments among the psychiatrists as to the modus operandi of the psychogenesis of these many disorders and disturbed by the dogmatism with which their pronouncements are made.

Such criticisms as inadequate research documentation, or improper controls, leveled at the psychiatrist or the psychosomatist are also applicable to the internist. Indeed, the gastroenterologist has been much too slow to appreciate the common association and interrelation of the personality and these disorders. Physiological research has been dominated by the morbid anatomy concept and not sufficiently integrated with personality and social studies. The most fruitful investigations have been carried out within the last 25 years by students in the fields of physiology, internal medicine, and psychiatry.

These specialists have pooled their studies and theoretical concepts to clarify the relationships of emotional influences to visceral activities Therefore, it would be presumptuous and beyond the scope of this paper to attempt an explanation of various clinical manifestations in which the clinician observes the relationship and strong influence of the psyche on physiological function. All illness must be considered a problem of disturbance of the psyche and soma, the relative influence depending on the dominance of one over the other.

Chairman's address, read before the Section on Gastroenterology and Proctology at the 105th Annual Meeting of the American Medical Association, Chicago, June 13, 1956

The purpose of this discussion is to reemphasize, by way of experience and example, the influence of emotion on the physiological functions of the patient in both health and illness. A trite statement—the abdomen is the sounding board of the emotions—is indeed apropos to our interest. In spite of our general knowledge of this relationship, and its common acceptance, it is surprising how little serious attention is given to this concept in the management of gastrointestinal disorders. No day passes in the activities of an office or hospital practice where problems of a physical nature can be adequately solved without proper evaluation of the psychic impact.

Emotion is commonly referred to in designating ways of feeling and patterns of action. As stated by others, it is a descriptive word representing three aspects: a subjective experience, a type of neurophysiological reaction, and a mode of behavior. The influence of the psyche on physiological behavior has long been recognized but poorly understood. Indeed, most of our concepts today are so closely related to pure speculation that it seems quite improper to take issue with any of them at this level of discussion. We need not argue the presence of psychic factors in illness. Experience and thoughtful observation prove this relationship beyond a doubt. For purposes of discussion, and as a general thesis of an internist, as expressed by Kubie, "psychological forces and somatic manifestations may have their roots in the same unconscious processes which discharge on the level of the psychic representation through thoughts and feeling, and partly on the physiological level through the autonomic nervous system."

Diagnosis and treatment depend much more on history than on other procedures. Careful laboratory studies should be made, to include x-rays, blood studies, stool research, and various metabolic evaluations, so that whatever of organic nature is wrong may be rectified. However, even in the hands of those skilled in these disorders, a personality study may reveal frank irregularities, yet not prove or substantiate them to be primary causes of gastrointestinal trouble.

It is quite impossible to explain adequately the causes of the various disorders of the gastrointestinal tract, in spite of our strong conviction that certain emotional instabilities are frequently present. At present, there are inadequate controls to justify the firm conclusions pronounced by the psychoanalysts; however, until such time as controlled research gives acceptable explanations, we, as internists, must go along, conscious of the emotional impact on the total organism. We must investigate hereditary predisposition, emotional immaturity, repeated psychic trauma, fatigue, frustrations, and fears. It behooves us to record a psychiatric evaluation, even if superficial, in all gastrointestinal disorders. I find it difficult to identify peptic ulcer or chronic ulcerative colitis personalities, yet I would not belittle an attempt to group certain characteristics that, in general, would be suggestive of them. What seems of particular importance is the recognition of certain methodology in dealing with the specific lesions and recognizing the influence of these characteristics on their causes and treatment.

I recall that I first found more adequate explanations for these previously inexplicable manifestations, explanations that emphasized the need for relating organic and functional disorders, in the works of Déjerine and Gauckler, who represented the thinking of the French school of early 1900 and, although lacking the present-day dynamic approach, provided much food for thought. I refer to their interesting presentation on the subject of emotion in gastrointestinal disturbances, because it is one of the early attempts to integrate functional disturbances with a primary organic disease or somatic dysfunction. Slowly this general understanding has become acceptable and is finding its way in the practice of psychosomatic medicine. The revived interest in psychological factors in medical disease is wholesome progress. That a functional disturbance of the stomach or intestine may in time lead to organic disease is a concept that is generally supported in observation and theory. Alexander says, "Anxiety sets in motion different psychological chains, the nature of which is one of the factors determining the type of physiological response that will ensue. Anxiety is not a specific factor in man, but he handles it in a manner characteristic of him."

Peptic Ulcer

Peptic ulcer is an organic disorder exhibiting a close relationship to the emotions. It is a lesion that may occur at almost any age in life. It is commonly found in persons between 15 and 30 years of age, coincident with a time of great instability, a need for understanding and adjustment, when the individual is especially responsive to the undercurrents of stress situations. The importance of psychogenic factors in the etiology of ulcer must be commonly emphasized. Prolonged frustrations, which cannot be adequately resolved, are present frequently in patients with recurrent peptic ulcer.

Physicians are well aware of the inception and exacerbation of ulcer symptoms under stress and fatigue. Increased incidence of acute perforation of peptic ulcer and massive gastric hemorrhage, as recorded by the British during the blitz of World War II, is a well-documented observation. Patients become increasingly conscious, after repeated experiences, that trouble with ulcers begins after bouts of worry or tension rather than after intemperate food indulgence. This would seem to justify the adage that it is not what you eat that causes the ulcer but what is eating you.

Cannon, Pavlov, Carlson, and others were among the first to demonstrate the production of gastric juice of high acid and peptic values through nervous-system stimulation. Minsky, and later Gray, have demonstrated the relationship between varying stresses and uropepsin formation and gastric secretion. The measure of gastric activity in this fashion gives more credence to a theory of relating stress and strain and psychic tensions to physiological manifestations. Wolff and Wolf, with their well-documented evidence, have proved a close relationship between functional disturbances and organic disease and between intense emotional stress and disturbed physiological function. Thus we may accept the proposition that stress from anxiety plays a causal role in the etiology of peptic ulcer. Whether we agree with Draper that "persistent fear and anxiety reaction is the primary emotional reaction" or that the subconscious neurotic conflicts are primary is not pertinent to this discussion. Somehow, an emotional conflict can almost invariably be found as a common denominator.

Individual information must be sought for the overall management of peptic ulcer. This need not be done by a psychiatrist, but by the internist who is willing to give adequate time. The psychosomatist can be more effective in a certain restricted group of patients, but, in the large percentage, the physician who has the patient's confidence and the interest to inquire will most likely succeed in securing information that adequately influences the therapy. Confidence, established at this level and area of management, is an invaluable asset.

Hematemesis and Intractable Ulcers

In other papers I have emphasized the influence of disturbed emotions on acute or recurrent hematemesis and intractable ulcers. When orthodox management incorporates an evaluation of the personality and stress situations of the patient with an ulcer, hemorrhages will be less, the intractable ulcer will occur less often, and surgical indications will cease to be dogmatically stated as "over a certain age, and having had so many hemorrhages." Chronic anxiety may precipitate sudden hemorrhage, and panic and fear have killed many a patient while under observation and treatment for massive hemorrhage. Why harass an exhausted patient in shock by having an inexperienced nurse take a blood pressure every hour? Has anyone instructed the nurse in taking and interpreting a pulse and in offering sound and positive reassurance to the patient? It is understandable that all customary procedures have their place, but to overlook one of the most important techniques—the proper psychological approach—is inexcusable.

Ulcer management includes proper diet, supplemental vitamins, neutralizing medication, and psychological evaluation. To my mind, it would be quite as improper to consider only the stress situations in the patient with ulcers as it would be to confine treatment to diet and antacids. The uncomplicated, relatively acute ulcer may well respond to a fishing trip, but the one complicated with recurrent hemorrhage or moderate obstruction with associated night secretion requires the full therapeutic management. A patient must not only learn to live with the ulcer but, of equal importance, how to live with it. To live with the ulcer implies an understanding of the psychic impact, and failure to anticipate a recurrence necessitates a formula of diet and medicine. Phenobarbital, sodium bromide, and the newer tranquilizing drugs help to control the states of tension that the physician has difficulty in combating. These may be the only means of controlling excessive secretion when the patient is in a highly emotional state.

Chronic Ulcerative Colitis

Chronic ulcerative colitis is another serious disorder in which the psychiatric component in the etiology is preponderant. Some years ago I was asked to see a 16-year-old boy with bloody diarrhea. Proctosigmoidoscopy revealed the characteristic friability of the rectal mucosa, with the minute multiple hemorrhages of chronic ulcerative colitis. The usual supportive measures had been instituted, including numerous transfusions. For the next six weeks there was gradual deterioration, associated anorexia, weight loss, anemia, and pyoderma. Innumerable bloody, watery stools were passed daily. The temperature ranged between 101 and 104 F (33.9 and 40 C), and dehydration became marked. Surgical and psychiatric consultation indicated divergent views. The family would not accept surgery but was willing to try psychotherapy. Fourteen days of local sanatorium supervision resulted in dramatic improvement. The temperature dropped to normal, the stools were reduced from 20 to 2 a day, and the patient began calling for food. His convalescence ran a remarkably smooth course. Hostility and a mother complex were finally clarified. This patient is now 34 years old, a father of two children, a graduate in dentistry, and a teacher in his specialty. He has occasional exacerbations, at which times the intestine is excessively active and the rectal mucosa is friable, returning to a fairly normal state after consultation but without specific medication. It has been my experience that therapy directed toward understanding the personal problems, rather than symptoms of the colon, will return the greatest success.

The patient I have referred to was managed prior to antibiotics and at a time when there were few sulfonamides. Today these drugs are effective in controlling complications. Cortisone and other steroids are used to advantage, particularly in the acute states. These supportive measures are important, but for management and guidance, in the long run, a familiarity with the patient's situational reactions is essential.

Functional Disorders

There are a number of disorders, classed as functional, that alarm the patient, confuse the physician, and, when not correctly managed, result in serious gastrointestinal invalidism. Among the more common may be mentioned nervous vomiting, anorexia nervosa, nervous diarrhea, constipation, and irritable colon. Difficulty in swallowing and unwillingness to eat in young and old patients are frequently observed. Nervous diarrhea, mucous colitis, spastic colitis, and irritable colon are different manifestations of the same basic condition. Family jealousy, parental domination, marital conflicts, family insecurity, fears, and frustrations are commonly associated with these abnormal disturbances.

If organic changes are absent, then the emotional component is the chief etiological factor. Almy has correlated constipation with defensiveness, hostility, courage, and adequacy and diarrhea with dependency, self-reproach, and fear. The stress of having desires frustrated acts on autonomic centers, resulting in disturbances in motility and secretions.

Comment

From the above discussions, might we not assume that consultation between social service department, psychiatrist, and internist should be practiced whenever these difficult problem cases appear? With that attitude in mind, the same philosophy may be expected to dominate the understanding and care of all patients. Briefly then, the examples and references noted above merely serve to emphasize the psychogenesis of gastrointestinal disease. The many classifications of disorders in this system will become unnecessary when there is a fuller appreciation of the constant interrelationship between psychological stress and physical manifestation. Intelligent management considers the human organism as an integrated unit where psychological stress and social maladjustments are given as much consideration as specific therapy to the end-organs.

Conclusions

Emotional stimuli may ultimately lead to a visualized organic lesion such as peptic ulcer or to dysfunction resulting in spasm or uncoordinated peristalsis in the intestine. The facets of psychological origin must be sought for and properly evaluated in treatment. In the field of gastroenterology the greatest success is obtained by study and treatment of the total organism.

636 Church St.

TO SOCIALIZED MEDICINE AND SOCIALISM BY WAY OF THE VETERANS ADMINISTRATION

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• *The medical program of the Veterans Adminstration shows a steady development from 1917, when the first purely medical benefits for veterans were authorized and limited to veterans with service-connected disabilities, to 1956, when the 170 VA hospitals have more than 123,000 constructed beds and more than 114,000 operating beds as compared with 37,570 patients with service-connected conditions and almost 66,000 with non-service-connected conditions. The course of this wasteful development must lead either to an inequitable situation in which one-third of the adult citizens are, while two-thirds are not, entitled to free hospitalization, or else to government hospital and medical care for the entire population. The unfair discrimination that now operates could be obviated by developing the present plan consistenly to its abhorrent conclusion, namely, complete government control over all personnel and services, with tax-paid, politically controlled medicine for everybody. The reasonable alternative is to reverse this trend as regards the VA program and to protect and improve our private system of health care for all people.*

Those of us concerned over the trend toward socialism in this country, and actively interested in stopping the spread of government control over the nation's medical services, have learned in recent years that we must be on guard against a wide variety of dangers. Some of them are obvious, outright threats, bearing all the earmarks of socialistic thinking. Others, which are more subtle and insidious, require careful study of their future effects and implications. To put it in military terms, we have learned that we must be vigilant not only against frontal assaults but also against flank attacks and infiltration tactics.

An outstanding example of the frontal assault was the attempt in 1949 to push through the Truman-Ewing plan for a system of national compulsory health insurance. The medical profession launched a vigorous campaign against that proposal, took the facts to the people, and mobilized effective, articulate support from an overwhelming majority of the American citizens. Since the failure of the big frontal assault, there have been many examples of the flank attack. These are found in the countless so-called fringe measures that, in effect, would intrude the federal government into medical education, voluntary health insurance, medical care for the dependents of military personnel, construction of private medical facilities, and a wide range of other medical activities, all of which should be left with the states, local communities, and private groups of individuals. These "fringe" proposals, by extending federal control a bit here and a bit there, add up to a tremendous step toward socialization.

It is not enough to be on guard only against new proposals, whether they be obvious or subtle, which would move us in the direction of socialized medicine. There is still another kind of danger that we might call a sort of mental or philosophical subversion of good intentions. This danger arises when a familiar homegrown American program suddenly takes on a new meaning, a new and dangerous significance. We look about us and realize that right here in our own back yard, without any prodding from planners and socializers, we have allowed politicians to create a Trojan horse of ominous dimensions. The best example of this type of danger is the hospital and medical care program of the Veterans Administration. This program, with the passage of time and changing conditions in America, has been allowed to drift far from its original humanitarian purpose. Today, because we as a nation have failed to keep a tight rein on the legislative philosophy behind that program, it now constitutes the biggest single mechanism that could nudge us toward government-controlled, tax-paid medical care for the entire population. To illustrate my point, I should like to quote two brief paragraphs from the 1955 report of the Hoover commission's task force on federal medical services. The task force said in its preface:

> If only because of their increasing number, variety and magnitude, the medical services maintained by the Federal Government call for appraisal of their organization. But the case for critical review is cogent for another reason. Whatever inclines any one Federal medical service to diverge from all others provides thereby a reason for review lest it become first a law unto itself and later beyond any control. The circumstances that favor differences and divergences are many.

Read before the annual meeting of the Louisiana State Medical Association, April, 1956.

> These Federal medical services have come into being at different times during the past 150 years: Thus each has its own history and tradition. They have had different rates of expansion. They have all changed and are still changing, in both reputed and real significance. They have different motives and serve different main purposes.

More than any other federal medical agency, the VA hospital and medical program has become "a law unto itself," a sort of sacred preserve that some people seem to feel should not even be examined or questioned by the American taxpayers who pay the bill. More than any other similar program, it already has gone beyond reasonable control. More than any other, it has changed radically "in both reputed and real significance." Therefore, let us look at the history and growth of the VA program, to see how all this has come about, to appraise the present, and to predict the future. The situation has reached the point where the American people must make a national policy decision affecting not only veterans but the entire population, present and future.

Expansion of Original Program

To begin with, it should be emphasized that the original motive of the veterans' medical care program was the desire to provide care for any veteran who had become disabled in the course of service to his country. That was, and still is, a sound, humanitarian purpose and a legitimate obligation of the federal government. Over the past 33 years, however, as a result of politically motivated acts of Congress, the program has been expanding primarily to provide care for a veteran with a disability that occurred after his discharge from military service and that has no relation to military duty. Emphasis has shifted from the care of service-connected conditions to the care of disabilities that do not originate in military service.

Contrary to some statements and claims, there is no historical precedent or American tradition justifying such a governmental program. The first purely medical benefits for veterans were authorized by the Congress in 1917 in an amendment to the War Risk Insurance Act. The medical services and supplies provided by that legislation were limited to veterans with service-connected disabilities. The Veterans Bureau, superseded by the Veterans Administration in 1930, was created by an act of Congress in 1921, and the following year the new agency took over a number of U. S. Public Health Service hospitals that had been caring for veteran patients.

The first authorization for the care of any kind of non-service-connected cases came in 1923. It occurred then because a reduction in the load of patients with service-connected conditions had made some beds available. As a result, the Congress authorized hospital care for certain veterans of the Spanish-American War, the Philippine Insurrection, and the Boxer Rebellion. The veterans involved were those with neuropsychiatric or tubercular diseases, whether service-connected or not. Although this legislation affected a comparatively small number of veterans, it nevertheless soon required the construction of additional hospital facilities. Since then the ball has been rolling steadily, nudged along by vote-conscious politicians. The door's were opened much wider with the passage of the World War Veterans Act in 1924. This legislation restated the hospitalization provisions of the amended War Risk Insurance Act of 1917. It also provided liberalized hospital privileges, whenever existing government facilities were available, to a veteran of any war, military occupation, or expedition since 1897, regardless of the nature or origin of his disability. By 1926, 17% of all patients in veterans' hospitals were receiving treatment for diseases or injuries not related to military service.

The doors of the veterans' hospitals were swung completely open by the act of July 2, 1926, which eliminated the 1897 date and extended the benefits of the World War Veterans Act to the veterans of any war, military occupation, or expedition. This amendment qualified approximately 5 million veterans for lifetime medical care at public expense. The result was a huge influx of veterans into government institutions and a further acceleration in the construction of hospital facilities not needed for persons with service-connected cases. By 1928, non-service-connected cases were accounting for 49% of the admissions to veterans hospitals, and by 1931, that figure was up to 71%. In 1933 Congress passed a law known as the Economy Act of 1933 that repealed all previous public laws granting hospital or medical treatment or domiciliary care to veterans who served in or after the Spanish-American War. This law and its subsequent amendments provide the basic legislative authority for the current medical program of the Veterans Administration. The most important amendment, relative to non-service-connected disabilities, came in Public Law 141 of 1934, which provided:

> Any veteran of any war who was not dishonorably discharged, suffering from disability, disease or defect, who is in need of hospitalization or domiciliary care, and is unable to defray the necessary expenses therefor (including transportation to and from the Veterans Administration facility) shall be furnished necessary hospitalization or domiciliary care (including transportation) in any Veterans Administration facility, within the limitations existing in such facilities, irrespective of whether the disability, disease or defect was due to service. The statement under oath of the applicant on such form as may be prescribed by the Administrator of Veterans' Affairs shall be accepted as sufficient evidence of inability to defray necessary expenses.

By 1944, veterans' hospital construction had cost 218 million dollars since World War I, and 80% of all admissions during that time had been for treatment of non-service-connected disabilities. In that same year, Gen. Frank T. Hines, then administrator of veterans' affairs, pointed out: "The right of war veterans to hospital treatment for non-service-connected disabilities was initially founded upon the theory that there would be a certain number of vacancies in hospitals acquired and maintained for care and treatment of those having a service-connected injury or disease, and such right has always been conditioned upon available facilities."

For more than 30 years, even in the period immediately after World War II, the VA hospitals have had more than enough beds to care for all persons with service-connected conditions. Nevertheless—and despite the legislative limitation concerning available facilities—the VA hospital system has been continually expanded. What has happened, of course, is simply a constant increase in the number of extra facilities available for non-service-connected cases. This, in effect, distorts the real intent of the basic legislation, not to mention the original purpose of the whole program.

At this point I should like to emphasize four salient facts to help bring this whole problem into better perspective and sharper focus: first, the legislation governing the present VA hospital and medical care program was enacted 22 years ago, when we had less than one-fourth as many veterans as we have today. Second, we now have more than 22 million veterans, living and aging at a time when the nation has been seriously infiltrated by the ideas of the welfare state, and by the philosophy of "let Uncle Sam do it." Third, no legal, binding, ironclad limit has ever been placed on the extent of existing VA facilities, or on the amount of money that Congress can appropriate to build new facilities. And fourth, the facts and philosophy behind the VA program have never been brought clearly to the attention of the American people, who have never given a mandate for the type of operation that has developed.

Cost and Size of VA Program

What has developed? What is the present size and cost of the VA program? This is a problem in which the truth is found in the black and white figures of reports and surveys, so let us look at some of the major facts that emerge from the mass of statistics. In 1936 the VA hospitals had just under 45,000 operating beds. That was already 2,400 more beds than were needed for all persons with service-connected cases in these hospitals on Nov. 30, 1954, 18 years later. At the end of the 1940 fiscal year—and that, mind you, was almost a year and a half before Pearl Harbor—the VA was up to almost 59,000 operating beds, an increase of 14,000 over 1936. The increase alone was greater than the number of patients with non-service-connected conditions in the hospitals at that time. By the end of the 1950 fiscal year, there were more than 106,000 operating beds, but less than 35,000 patients with service-connected conditions. By the end of the 1954 fiscal year, according to the recent Hoover commission report, the VA had 170 hospitals, not including contract hospitals, with more than 123,000 constructed beds and more than 114,000 operating beds. They had at the same time only 37,570 patients with service-connected conditions and almost 66,000 with non-service-connected conditions.

You will note that in less than 20 years there has been an increase of almost 70,000 operating beds that are not needed for patients with service-connected conditions and are used only for those with non-service-connected conditions. The VA program, as presently authorized, is scheduled to reach 174 hospitals with about 126,800 beds, at which point it is supposed to "stabilize." This myth of "stabilization," of course, is the same old story that has been handed out for the past 20 or 30 years by politicians who, in practically the next breath, start asking for more VA hospitals, more beds, and bigger appropriations.

The number of VA hospitals, beds, and patients in those beds on a given day tells only part of the story. The one-day-census method, which the VA prefers and which puts the VA program in the best possible light, proves in itself that the care of persons with non-service-connected disabilities has become the predominant part of the program. However, when we look at the admissions and discharges in VA hospitals in a whole year's time, we get an even clearer picture of what has happened. For example, during the 1934 fiscal year fewer than 64,000 veterans were admitted to VA hospitals and homes. In the 1951 fiscal year the VA treated and discharged over half a million veterans, 512,000 to be exact, and almost 85% of them had non-service-connected disabilities. Seventy-six per cent of those half-million veterans had non-service-connected general medical and surgical disabilities, as distinguished from tuberculosis and neuropsychiatric conditions.

The figures supplied by the VA in June, 1955, and confirmed by VA Administrator Harvey V. Higley, show that persons with non-service-connected cases accounted for over 62% of the patient load on Nov. 30, 1953, and over 61% on Nov. 30, 1954. VA figures also show that in the 1953 calendar year the VA hospitals discharged over 460,000 patients, more than 83% of whom had disabilities not connected with military service. Over 70% of them had been treated for general medical and surgical conditions that had no relation to the time spent in military service. And what about the increase in the cost of the VA hospital and medical program? In 1934 it cost just over 37 million dollars, while in the 1955 fiscal year it cost over 750 million dollars. The VA budget for the 1956 fiscal year is 790 million dollars, not including hospital construction.

I want to underline three basic facts brought out by these statistics. During the past 20 years, the number of VA hospital beds almost tripled; the number of patients treated each year has increased from seven to eight times; and the annual cost of the program has increased more than 20 times over and is fast approaching the 1 billion dollar mark. I ask you, how big must a federal medical program get before it is considered "beyond control" and of "changing significance" and before the American people put a bridle on its size, cost, and philosophy of operation?

Many people in this country, both veterans and nonveterans, believe that the VA program already is too big, and that the time for action is now. Two groups in particular—the American Medical Association and the Hoover commission's task force on federal medical services—have made careful studies of the problem and have developed specific recommendations. Before I discuss the current trends and probable future growth of the VA program, let me outline the findings of those two groups.

A. M. A. Policy

The policy of the American Medical Association is expressed in the committee report adopted by the A. M. A. House of Delegates in June, 1953.

> Your Committee recommends with respect to the provision of medical care and hospitalization benefits for veterans in Veterans Administration and other federal hospitals that new legislation be enacted limiting such care to the following two categories: (a) Veterans with peacetime or wartime service whose disabilities or diseases are service-incurred or aggravated; and (b) Within the limits of existing facilities to veterans with wartime service suffering from tuberculosis or psychiatric or neurological disorders of non-service-connected origin, who are unable to defray the expenses of necessary hospitalization.

> Your Committee recommends that the provision of medical care and hospitalization in Veterans Administration hospitals for the remaining groups of veterans with non-service-connected disabilities be discontinued and that the responsibility for the care of such veterans revert to the individual and the community, where it rightfully belongs

I cannot emphasize too strongly that there has been no change in A. M. A. policy regarding patients with service-connected disabilities. The best possible care for these veterans is clearly a national responsibility. The A. M. A. policy statement said on that point, "Your Committee would like to stress the fact that these recommendations do not suggest any limitation or impairment of the hospitalization or medical care now available to veterans who have become physically handicapped as a result of military service. We are in complete accord with that program."

On the second point, the care of war veterans unable to pay for the treatment of non-service-connected tuberculosis or neuropsychiatric disorders, the A. M. A. policy statement said:

> The recommendation of the Committee with respect to the treatment of veterans with tuberculosis and neuropsychiatric disorders of non-service origin in federal hospitals is believed necessary at this time because of the inadequacy of local facilities designed to provide treatment for all such cases It is the feeling of the Committee, however, that the entire question of whether the care of these patients is a local or a federal responsibility must be reanalyzed by the Congress. The rapidly expanding veteran population and the need for facilities for the remainder of our citizens afflicted with these diseases suggests that community facilities must be developed under state or local administration for the benefit of all. Preferential treatment for veterans with these non-service-connected disabilities cannot be continued indefinitely, in view of its detrimental effect on the health and the economy of the entire nation

The remaining groups of non-service-connected cases, which the A. M. A. believes should now become the responsibility of the veteran himself or his community, are the general medical and surgical conditions, whether they be chronic or nonchronic. These, if you remember, accounted for 76% of all the VA hospital discharges in the 1951 fiscal year, and over 70% of all the discharges in the 1953 calendar year. I can best sum up the A. M. A. position with one more excerpt from the official policy statement:

> The medical profession must concern itself, not with the number of chiselers in Veterans Administration hospitals nor with the efficacy of the Veterans Administration in the administration of enabling legislation, but rather with the broad question of whether such legislation is sound, whether the federal government should continue to engage in a gigantic medical care program in competition with private medical institutions, and whether the ever increasing cost of such a program is a proper burden to impose on the taxpayers of the country. A consideration of this problem must of course be predicated upon a concern for the health of the entire population and not just a particular segment

Hoover Commission Recommendations

The soundness of the A M. A. position was borne out by the 1955 report of the Hoover commission's task force on federal medical services. That report pointed out that of the 21 million veterans in the United States, only 3,500,000 had some service-connected disability; the remaining 17,500,000 had no such disabilities. The task force also estimated that the total number of veterans eligible for war-service benefits would reach a peak of about 24 million in the next three years. In a report containing many facts and figures that demonstrated the uncontrolled expansion of the VA program, the task force had this to say:

> The Veterans' Administration needs a firm legal basis for determining the eligibility of veterans for medical care. The Federal Government has an obligation to care for veterans who have incurred disabilities in service For such veterans, this obligation is of a continuing nature and requires the highest obtainable quality of medical services. But responsibility for the care of veterans with non-service-connected disabilities is not of the same order. Lifelong care should not evolve alone from the very normal incident of fulfilling the duties required of every citizen

The task force recommended that "all existing rules, regulations, executive orders, and laws relating to veterans or veterans' benefits, and in particular to medical treatment and domiciliary care benefits, be consolidated and enacted into a single, all inclusive, comprehensive code." It also recommended that Congress enact legislation to provide that veterans may receive "(a) hospital care for non-service-connected disabilities if medical need for such disabilities was established within three years after separation from service, and (b) outpatient care following hospitalization for those non-service-connected disabilities for which medical need was established at the time the veteran was hospitalized."

The task force estimated that the three-year time limit on establishing eligibility for the care of non-service-connected conditions would immediately reduce the federal government's responsibility from a potential of 21 million veterans to about 7 million, including 3,500,000 with service-connected disabilities The suggestion for outpatient care, if applied within the framework of the three-year time limit, would help to reduce the length of hospital stay, decrease the cost of care, and permit more efficient use of existing facilities Strangely enough, the Hoover commission accepted the task force recommendation on outpatient care, but it did not adopt the proposal for a three-year time limit on establishing eligibility. This, in effect, would open the doors for lifelong outpatient care of non-service-connected disabilities, and would skyrocket the costs of the VA program. It is still a mystery of logic how the parent commission, whose purpose is to save money for the taxpayers, ever arrived at such a paradoxical conclusion

The medical task force also recommended "that Congress authorize no further construction of Veterans' Administration hospitals, and that the Veterans' Administration close and dispose by sale or otherwise any hospital which, in its judgment, can no longer be operated effectively or economically." The Hoover commission accepted those recommendations, and it also recommended that the veteran's statement of his inability to pay for hospitalization should be subject to verification This, of course, is only a halfway measure that does not come to grips with the basic philosophy of the current legislation. Both the task force and the parent commission made additional technical recommendations designed to tighten the administration of the VA program, improve its efficiency, and reduce its cost.

Inefficiency in VA System

There are countless examples of inefficiency, waste, and duplication in the VA hospital construction program and in the over-all operation of the VA system. As just two examples, I want to cite briefly the main facts emerging from two recent surveys in different parts of the country. One concerns the "Home Town" care program that is in operation in some states. Under this type of plan, veterans with service-connected disabilities can obtain outpatient care from private physicians at federal expense. In California, according to a study by the California Physicians Service, a monthly average of 12,000 such veterans get outpatient care from California Physicians Service physicians, and 7,400 get it in VA clinics. Using the San Francisco-Oakland Regional Office VA clinic as a basis, the figures for the 1954 fiscal year show that the average monthly cost was $23.15 for the veterans treated in the VA clinic, as against only $15.40 for the veterans receiving care from California Physicians Service physicians. The cost for each visit was $11.38 at the VA clinic, as against only $5.90 in the physicians' offices. The survey indicated that "Home Town" care for all California veterans with service-connected conditions could save the VA at least $688,000 every year, not to mention the saving of time and money for the patients themselves.

The second survey, by the Cincinnati branch of the National Medical Veterans Society, concerns VA hospital construction policy in that Ohio city. According o this survey, two VA hospitals already serving the incinnati area have 632 beds authorized for general medical and surgical cases but not in use. Even excluding these, there is no shortage of general beds in he area. However, the VA does have an acute need or more neuropsychiatric beds in that area, and Cincinnati could staff such a hospital. Yet the VA is determined to open the Cincinnati VA hospital as a general medical and surgical facility, which will not meet the actual needs of the veterans and will aggravate health personnel shortages already existing in the area.

Regardless of all the statistics indicating waste and extravagance, these are only symptoms of the underlying trouble. The real question involves the basic egislative philosophy behind the program. The VA has to administer its hospital and medical program in accordance with existing laws and the financial directives of Congress. And regardless of whether one agrees specifically with the policy of the American edical Association, or the recommendations of the oover commission or its medical task force, the fact remains that there is mounting concern in this country over the implications of the VA program. That concern is predicated not only upon the gigantic size of the present program but also upon current trends pointing to even greater future growth.

More Expansion Possible

One of the most important single factors is the aging of our veteran population. By 1970—only 14 years from now—the VA estimates more than 86% of the living veterans discharged before June, 1950, will be 45 years of age or older, as compared with a fraction under 23% in 1952. In actual numbers there will be almost 14 million at or beyond age 45, more than three times as many as there were in 1952. At the same time, almost 13% of these pre-Korean-war veterans will be age 65 or over, as compared with only 3% of all veterans in fiscal year 1955. That is, there will be over 2 million veterans at or beyond age 65, more than 10 times the number in 1952 and 3 times the number of all over-65 veterans in June, 1955. Past experience of the federal government shows that as veterans grow older, and more vulnerable to chronic ailments, there is a constant increase in the total patient load of VA hospitals, in the proportion of non-service-connected cases, and in the average length of hospital stay. Unless we change our national policy, these factors will produce a tremendous future rise in the size and cost of the VA program.

Such an expansion was predicted in 1945, five years before the Korean conflict, by Gen. Frank T. Hines, then administrator of veterans affairs: "With the numbers involved in this war and with the needs clause retained in the legislation, a peak load requirement of some 400,000 beds by 1975 would seem a fair estimate. With the needs clause removed the number would be measurably increased to the extent that free hospitalization would be afforded by the government for approximately one-third of the adult citizens of the country, which in turn might involve a recurring annual expenditure for such an item alone of approximately $1 billion."

More recently, in 1952, the VA department of medicine and surgery prepared a report for the Booz, Allen & Hamilton Company, which was making a management survey of the agency. In that report the VA itself estimated that, if present trends and admission policies continue, the VA by 1975 will need 265,960 hospital beds and 78,500 domiciliary beds to support the anticipated patient load. That is a total of almost 350,000 beds.

In addition to the size and aging of our veteran population, other trends and influences are affecting, or can affect, the future expansion of the VA program. One of these, which was officially condemned by the A. M. A. House of Delegates in June, 1954, is the practice of establishing a "presumption" of service connection for veterans' disabilities by means of legislative action rather than by scientific medical examination. Under this practice, a condition is presumed to be service-connected if it occurs within a certain length of time after discharge from service; about 30 specific disabilities have already been included. At every recent session of Congress, many such bills have been introduced, and more and more of them became law. This, in effect, is simply an indirect method of increasing the VA load of non-service-connected cases. The end-result of this dangerous trend could well be for Congress to declare all veterans' ailments service-connected and therefore eligible for complete care with no questions asked.

We can reasonably expect in view of past experience that there will be continuing political efforts to broaden the benefits and loosen the eligibility requirements for veterans themselves. We also can expect politically motivated attempts to extend the VA hospital and medical care program to persons other than veterans. In fact, bills already have been introduced in Congress to provide such care for the dependents of veterans, and that would mean additional millions of government beneficiaries. We can expect, if the nation adopts a program of universal military training, that there will be inevitable political pressures to extend VA benefits to those who have completed such training. And, of course, if we have any more "small" wars like Korea or if we should be so unfortunate as to have another global conflict, then our veteran population will again increase rapidly, and the entire problem will be compounded many times over.

Future Course

When and where does the growth stop? When and where are the various trends checked? In my opinion, the time is now, and the job must be done in the halls of Congress, under the impetus of American public opinion.

The Hoover commission pointed out that the federal government already has undertaken responsibility for all or part of the medical care of about 30 million people. From the standpoint of potential beneficiaries, the VA medical program is by far the largest in the federal government, with 21 million beneficiaries now and an estimated 24 million within the next three years. From the standpoint of cost, the VA medical program is second only to that of the Defense Department, and its budget is approaching a figure of 1 billion dollars a year.

Through the VA program, we already have socialized, tax-paid, government-controlled medicine for one-eighth of our population. All they have to do is apply for it and claim that they are unable to pay for their own care. But what one section of the population gets from the federal government, the rest are likely to want in the near future, and there always will be plenty of vote-conscious politicians around to demand it for them. So what is the next step? Government hospital and medical care for the dependents of veterans?—for industrial workers?—for white-collar workers?—for farmers?—for old people?—for everyone with an income under $5,000 a year?—for the entire population? Where does it stop? Remember that in several countries, Germany and Great Britain for example, government medicine started out covering limited segments of the population, and ended up as full-fledged socialized medicine for all.

Through the VA program we are rapidly creating two classes of citizens with respect to hospital and medical care, those who once wore a uniform and those who did not. If we wait too long, and if we choose the wrong way to correct that unfair discrimination, we will be led down all kinds of socialistic byways. Through the VA program and its ever-mounting costs, we are constantly increasing the tax burden on all citizens, including veterans themselves. We can be taxed into socialism as well as legislated into it. Through the VA program we are siphoning off personnel and facilities needed to develop adequate health facilities for all the American people, including the veterans and their families in their home communities. If this trend is allowed to continue, our private system of medicine will suffer increasingly severe shortages, and the pressures will mount for complete government control over all personnel and services, to solve all problems and to simplify the entire system.

We, and I mean all of the American people, must decide soon, before it is too late, what is to be the future course of the VA hospital and medical care program. That decision will determine whether we protect and improve our private system of health care for all people or whether we eventually reach socialized medicine by default.

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SURVEY OF ONE HUNDRED CASES OF WHIPLASH INJURY AFTER SETTLEMENT OF LITIGATION

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• *One hundred patients with previously diagnosed cervical neck strain following auto accidents whose litigation on compensation claims had been settled were queried as to their present clinical status. After legal claims for damage were completed, 88% showed recovery, and over half of these had no residual complaints. Many emotional factors, but especially those concerning monetary compensation, greatly confuse proper medical evaluation and appear to be the cause of the wide divergence of professional prognostic opinions relative to this particular injury.*

Some months ago we neurosurgeons practicing in Memphis, Tenn., became increasingly concerned about the poor results in the treatment of the so-called whiplash type of injuries of the neck; we also became more concerned about the medicolegal implications that followed these types of injuries. The methods of treatment seemed relatively ineffective in many instances and were often complicated by a long period of chronic symptoms. In addition, we found that, when a neurological surgeon was called to give a medical opinion incidental to legal settlement of the accident, there was a wide divergence among the surgeons as to the severity of the injury and as to the future prospect of health. The neurosurgeon was often called to give a deposition or go to court for a defendant individual or insurance company and was expected to render an opinion as to the severity of the symptoms, the length of time that symptoms might persist, and further treatment that might be necessary and to give the degree of partial or total disability.

From the Department of Neurology, University of Tennessee.

Read before the Section on Nervous and Mental Diseases at the 105th Annual Meeting of the American Medical Association, Chicago, June 14, 1956.

In almost every instance another neurosurgeon, one of our colleagues, had also been called to testify for the plaintiff and to render opinions about the same condition, but to his consternation there seemed to be a wide divergence of opinion as to the important factors—again, namely, the type of treatment necessary, the length of time treatment was needed, the various appliances such as traction or neck braces that were indicated, and the possibility of surgery in the future if symptoms persisted. Psychoneurotic symptoms were so prevalent and seemed to be such a dominant factor in these cases that proper evaluation seemed even impossible and tended to underscore, so to speak, the physicians' difficulty in reaching a degree of unanimity of opinion.

In attempting to evaluate and render an opinion that had some validity, we found no adequate follow-up study in the medical literature that was of help. We decided, therefore, that there was a need for a study of cervical neck strains, or so-called whiplash injuries, but that this should be limited to those cases in which the problem of compensation and litigation had been concluded. In this manner, the psychosomatic symptoms could be more ably evaluated and the true degree of the chronic permanent symptoms and final disability more adequately determined.

Analysis of Symptoms

Most neurosurgeons are aware that cervical neck strains are usually caused by automobile accidents in which an occupant of a car, waiting at a traffic light, has his car struck forcefully from behind or from the side. His body is suddenly thrust in a position of acute flexion, followed by extension of head and with more than one oscillation of the head on the neck. To be exact, a matter of quick deceleration occurs, without time for reflex protective fixation of the cervical muscles. The effect of this rapid deceleration is to cause a stretching of the muscles and ligaments of the neck and possibly some edema, hemorrhage, and even direct rauma to the nerve roots. Indeed, we have one patient in whom x-rays revealed evidence of hemorrhage, as noted by a pharyngeal bulge. In addition, there may occasionally be injury to the intervertebral disk, with narrowing of the foramen, and subsequently it is possible that fibrosis and abnormal motility of the vertebral oints may occur. Granting the severe traumatic possibilities, we observed that in most instances the initial evidence of injury seemed trivial or minor, and, indeed, many times the patient, himself, belittled the njury, saying, "I did not think I was hurt" or "I hought nothing of it." He continued on his way, only to have symptoms develop several hours or even days later. In such instances, where there was little or minor vidence of trauma upon physical examination, chronic, persistent symptoms unresponsive to treatment frequently occurred.

Briefly, the symptoms were usually of a pattern. In the acute stage—at the time of the accident—the sensation of being dazed or bewildered was followed in a few minutes to several hours later by headache and nervousness, with neck soreness and tenderness. With these symptoms there were rather rapidly associated profound emotional reactions such as nervousness, instability, insomnia, and sweating of the hands. Many times the symptoms grew progressively worse over a period of weeks, although this was inconsistent with pathological possibilities. The findings by examination were variable in the acute stage. Often there were no objective disabilities, or there might be muscle spasm, fixation of the head and neck, and straightening of the cervical curve as evidenced by or confirmed by x-ray. However, the fact that the symptoms did not adjust to treatment or that they at times would even get worse, but improved after settlement of claims, cast doubt in our minds on the validity of the symptoms and rendered proper opinion by the physicians next to impossible.

Study and Findings

As a result of these problems in the evaluation of this type of injury, we felt that a thorough study of these cases, subsequent to the settlement of compensation or litigation claims, was indicated. Accordingly, funds were obtained to study this problem, with particular reference to symptomatology of whiplash injuries subsequent to the settlement of legal claims. All nine neurological surgeons doing private practice in Memphis cooperated and submitted cases of patients that were suitable for the study with whiplash types of injuries who had been treated or examined by them. A comprehensive questionnaire regarding symptoms, physical disability, attitude toward settlement of litigation, and symptoms subsequent to settlement of litigation was prepared. A fourth-year medical student was obtained to interview the patients and was given their names without other knowledge of the cases. Two hundred nineteen cases were submitted by the neurological surgeons; the student interrogator was able to have personal interviews with and to complete the questionnaire on 100 patients. The purpose of this paper, therefore, is to summarize, review, and record the results of these findings.

The analysis indicates that, out of 100 patients interviewed after settlement, 54 admitted that they were having no appreciable trouble at the time of the interview. None of these 54 patients had considered any of the symptoms serious enough to warrant a visit to a physician within the previous year, which was from 1 to 26 months after settlement of claims for injury. Thirty-four patients reported some minor discomfort on damp, cloudy days; this was manifested by such minor symptoms as pain on doing unusual exercises or unusual lifting, which might or might not be related to the previous injury. Some patients thought that they might have slightly more frequent headaches than prior to the accident. Patients 60 years of age or more showed a much slower recovery than those in the younger age group, and they felt that they had some mild arthritic symptoms possibly related to the injury; these patients are included in this group of 34 with mild residual symptoms.

In the 88 patients mentioned above, the greatest percentage of recovery was during the first year. Thirty-seven per cent of these patients required or were hospitalized for treatment. Many who had some minor complaints of pain admitted upon questioning that they had not followed medical advice as to medication, exercises, limitation of work, or returning for evaluation. A total of 12 patients, in spite of settlement of claims or litigation, appeared to continue to have enough trouble to be wearing Thomas collars, sleeping in traction, taking physical therapy or heat treatments, and periodically visiting a physician for help. Of these 12 patients, 5 had admitted that they refused to carry out the doctor's instructions as advised, in that they refused to modify their activities, rest or sleep in traction, or take physical therapy. Surgery was performed on only 2 patients out of the 100 interviewed, and they were asymptomatic except for slight limitation of motion of the neck.

Of the above group of 88 patients, 85 had liability claims ranging from simple settlements by insurance companies to law suits filed and appealed to state and supreme courts. Of these 85 patients, 49 were satisfied with the settlement and 36 were not. Of the 49 patients who were satisfied with the settlement of their claim, 29 had no significant symptoms at the time of the interview, 11 had only occasional discomfort, and only 4 were still having trouble enough to sleep in traction or occasionally wear a Thomas collar. Of the 36 patients who were not satisfied with their settlements, 9 were cured or had no subsequent symptoms, 20 complained of minor symptoms, and only 7 were having enough trouble to occasionally sleep in traction or to wear a collar. Of the nine patients who had no recourse to claim, that is, their case was not considered one in which they were entitled to compensation or settlement of a liability claim, six were having no trouble whatsoever, two were having minor complaints, and one had moderately severe symptoms.

Subsequent to settlement of legal claims, only three patients lost as much as six months from work or their usual occupation. This includes one patient who has been disabled three years. Only four other patients lost as much as three months' time; all others either lost no time or only a few days from their usual occupation. This compares to 26% who lost six months' time or more prior to settlement and 15% who lost as much as three months from work prior to settlement, making a comparison of 7% losing as much as three months from work after settlement against 41% prior to settlement of claims. While we recognize the comparison is open to some criticism, one cannot help but deduce that settlement of claim definitely influenced the symptomatology advantageously.

Comment

We were forced by the survey to draw certain definite conclusions in regard to psychosomatic symptoms that had developed in a considerable number of these patients. The interrogator, in his interviews with the patients, came to the conclusion that in some instances there were indications that the injury was being used by the patient as a convenient lever for personal gain, so to speak, though not necessarily on a conscious level. These instances were the forcing of a reluctant spouse to pay for household help or insistence on an air conditioner, a new car, a new house, or a vacation in Florida. After the litigation, some patients divorced and remarried; others bought new homes, redecorated the home, and bought new cars. Such changes indicate the possibility that the illness had been used as a means of implementing psychological or other adjustments that had previously been postponed or that, because of financial difficulties, the patient had not been able to fulfill. Our survey indicated that some patients who complained seemed to have developed through the injury an outlet or excuse for avoiding unpleasant tasks and a means of securing recognition from other members of the family and attention from neighbors, friends, and children. This was not thought by the examiner to be entirely on a conscious level, though it may have been conscious in the early stages. On the other hand, it must be noted that some patients financially were actually worse off, having lost their jobs due to being away from work too long in trying to complete law suits or actually feeling that they could no longer do the same type of work.

The conclusion that we draw from this study of 100 patients whose cases have been to a great extent freed of litigation or compensation claims is that the emotional factor plays an important part in the ability of the physician to obtain a satisfactory result from treatment. There seemed every reason to believe that the personal reaction of the patient to his injury complicated the evaluation of his symptoms, treatment, and recovery. The apprehension, nervous tension, and anxiety that these patients developed subsequent to the injury, as a result of fear for future health and as a result of the litigation, tended to accentuate the formation of a profound post-traumatic neurosis. This profound emotional reaction depended to a great extent upon the personality pattern of the patient, as well as the degree of his physical injury. Once the psychoneurotic symptoms had developed, they persisted for many months and were refractory to treatment, being finally resolved to a great extent by settlement of the litigation. It was for this reason that the evaluation of the history, examination, and permanent disability was at all times confusing and could only be made by such a study as we have concluded.

Summary

Of 100 patients with whiplash type of injuries who were interviewed subsequent to settlement of legal claims for damage, 88% have recovered, 54 with no residual and 34 with minor symptoms not requiring therapy. Twelve per cent continue to have severe symptoms, but only 6% of these are under medical treatment. Surgery was necessary in only two cases and was beneficial in both. Many psychsomatic symptoms developed and were manifested in some way in 85% of the cases. Loss of time for as long as three months occurred in 41% of the cases before settlement of claims but in only 7% subsequent to settlement of claims. The evidence indicates the great difficulty in evaluating whiplash type of injuries due to the complicating factor of monetary compensation.

22 N. Manassas St.

The following neurosurgeons cooperated in this study: Drs. R. E. Semmes Jr., Francis Murphey, C. D. Hawkes, E. C. Schultz, A. R. Tyrer Jr., R. L. DeSaussure Jr., B. W. Cannon, Robert Raskind, and William Ogle.

This study was supported by a grant to the Department of Neurology from the University of Tennessee School of Medicine.

The survey was performed by John R. McInnis, senior student, University of Tennessee School of Medicine.

MECAMYLAMINE IN TREATMENT OF HYPERTENSIVE DISEASE

OBSERVATIONS ON AN UNUSUAL NEUROMUSCULAR COMPLICATION

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• *Mecamylamine hydrochloride blocks conduction through autonomic ganglions and is presumed to be completely absorbed when given by mouth. It was evaluated in the treatment of 35 patients with severe hypertensive disease. The initial dose was 2.5 mg. given once or twice daily by mouth; subsequent doses were increased by 2.5 mg. every two days up to the individual patient's requirement for maintenance as determined by the standing systolic blood pressure and therapeutic response. The average daily maintenance dose for the 18 patients who responded with a significant reduction of the blood pressure was found to be 24 mg. (range 5 to 45 mg.). There were, however, 17 nonresponders. Of the 35, only one tolerated therapeutic doses without side-effects and 6 had to stop taking the drug. The others, though uncomfortable, were able to continue medication, in some instances, up to 12 months. The most frequent complaints were constipation, blurring of vision, xerostomia, and various symptoms of postural hypotension. Seven patients, including 5 from this group of 35, showed signs of an unusual neuromuscular disorder, with anxiety, tremor, and even convulsions, while taking the drug. Mecamylamine is considered to be a useful agent in the treatment of hypertensive disease. Its therapeutic advantage over drugs with similar ganglionic effects is small.*

The usefulness of the hypotensive properties of ganglionic blocking agents in the treatment of severe hypertensive cardiovascular disease has been widely established.[1] The therapeutic success or failure of autonomic ganglionic blocking drugs is dependent not only on the sensitivity of the individual patient to their hypotensive effect but also on the ease of administration and avoidance of untoward side-reactions. Erratic blood pressure responses, irregular absorption, and development of tolerance to readily available ganglionic blocking drugs have stimulated a continuing search for more effective antipressor agents of this sort.

Mecamylamine hydrochloride (3-methylamino-isocamphane hydrochloride) is unusual among ganglionic blocking agents in that it is a secondary amine rather than a quaternary ammonium compound. Further, it is believed to be completely, rather than fractionally, absorbed from the gastrointestinal tract[2]; in contrast to hexamethonium,[3] it appears to distribute in a volume of body fluid substantially larger than the extracellular fluid[4] and to be comparatively slowly and only partially excreted as such. Such a combination of properties should yield an agent that would elicit predictable, prolonged responses to oral doses. This would be advantageous, since erratic depressor responses to orally administered hexamethonium or pentolinium have been ascribed, in part, to variations in the fraction of the drug absorbed from the intestinal tract. These presumptions have been supported by previous clinical studies.[5]

We have observed the effects of mecamylamine in a group of patients with severe hypertensive disease, of whom some had had no prior antihypertensive therapy and others had been treated with potent antipressor drugs. The purpose of this report is to present the results of experience with mecamylamine in terms of the control of the hypertensive process, to offer comparisons with other antihypertensive regimens, and to describe what may be an unusual complication of the use of this drug in patients with advanced hypertensive vascular disease.

Method of Study

The group was composed of 12 women and 23 men, ranging in age from 28 to 62 years; the average age was 49 years. All 35 patients were given mecamylamine for at least one month, 13 received it for an additional 2 to 3 months, 7 for 4 to 8 months, and 3 for 9 to 12 months. Of these, 32 were hospitalized during the initial treatment period of one month or more. All who continued to take the drug for longer periods were seen at frequent intervals as outpatients. Blood pressures were measured four times daily with patients in the supine and standing positions by nurses in the hospital or by the patient or a relative at home.

Thirteen hospitalized patients had received no prior antihypertensive treatment; mecamylamine was not administered to these until weekly averages of blood pressures had been constant for two or more weeks, during which time the status of the patient was evaluated.[6] The majority (21) of the patients were restricting sodium intake to less than 2 gm. daily because of evidence of hypertensive heart disease. The diets were not changed during the study period. Twenty-two patients had received prior antipressor medication; of these one patient had been receiving thiocyanate, 6 reserpine, 5 hydralazine alone or in combination with reserpine, and 10 patients a ganglionic blocking agent (hexamethonium, pentolinium tartrate, or chlorisondamine chloride) alone or in combination with reserpine. Reserpine therapy was usually not discontinued in patients who were receiving it; however, mecamylamine was substituted for either hydralazine or the ganglionic blocking agent being used.

Of the 35 patients, 10 had severe essential hypertension and 10 presented the syndrome of malignant hypertension; 11 had residual essential hypertension with varying degrees of vascular damage, remission of a preexisting malignant phase having been accom-

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From the Division of Research, the Cleveland Clinic Foundation, and the Frank E. Bunts Educational Institute.

plished by previous treatment; and, in 4 patients with severe hypertensive disease (in 3 of whom the disease was in the malignant phase), the process was secondary to primary renal disease. The severity of the hypertensive disease was scored in terms of a composite severity index that rates from 0 to 4 points the extent of vascular disease in (1) heart, (2) kidney, and (3) brain, on the basis of clinical and laboratory study, as well as (4) the level of diastolic arterial pressure, to a maximum score of 16.[1b] The range of the severity index in the group of patients prior to administration of mecamylamine was 3.0 to 14.0 and the mean 8.4.

Response to treatment was classified according to average supine diastolic blood pressure. If this was maintained at less than 110 mm. Hg the patient was considered a responder and, if not, as a nonresponder. The data will show that 20 (57%) of the patients were considered as responders after one month of therapy and 15 (43%) were nonresponders.. The drug therapy was continued 2 to 12 months in 23 of the initial group of 35 patients; 14 (61%) of these 23 patients were then considered as responders and 9 (39%) were classed as nonresponders. Five patients (cases 36 through 40) not included in the group of 35 were observed during an initial period on mecamylamine therapy alone, after which it was given in combination with hydralazine. An additional two patients (cases 41 and 42) are reported on in detail because they exhibited an unusual complication during treatment with mecamylamine.

Dosage and Administration

The initial dose of mecamylamine was 2.5 mg. given in the morning only, or twice daily in the morning and early evening. A few patients whose tolerance to the drug was very small were able to secure uniform control of their blood pressure by taking one or two daily doses, but in most this was secured only by giving additional doses at noon and/or bedtime. The individual doses were increased by increments of 2.5 mg. each, every two days, according to the standing systolic pressure at the time of scheduled medication. The usual prescription was for the individual's maximum dose to be taken when the standing systolic pressure was more than 140 mm. Hg. A smaller (roughly two-thirds) dose was taken when this pressure was between 140 and 120 mm. Hg, and use of the drug was omitted when it was below 120 mm. Hg. Most of the patients attained a fairly stable level of maintenance dosage in the course of less than two weeks. The average maintenance dose in the whole group (at the end of the study period) was 39 mg. daily and ranged widely from 5 to 180 mg.; among the 18 responders at this time (1 to 12 months), this average was 24 mg. (range 5 to 45 mg.); and, among the 17 nonresponders, the average was 55 mg. (range 5 to 180 mg.).

The greatest fall in blood pressure occurred usually one-half to two hours after oral administration but, at times, was delayed for three or four hours. A significant hypotensive effect often persisted for about 12 hours; in some this interval was only 4 to 6 hours, and, in others, notably those in renal failure, it persisted for 24 hours or more. In general, responses to equal oral and intramuscular doses were approximately the same, allowing for the fluctuations in responsiveness and requirement shown by most patients. The day to day dosage requirement of mecamylamine was often quite variable for the same patient. Some individuals were able to take a fairly constant daily dose, but more showed considerable fluctuation in the amount of drug necessary to maintain a reasonably constant blood pressure level. In general, this range of variation in daily dosage requirement of mecamylamine was comparable to that for other ganglionic blocking drugs for the same patient (table 1).

Results

Administration of Mecamylamine to Previously Untreated Patients.—All of the 13 patients who had not previously been given antihypertensive drugs showed at first a significant fall in supine diastolic blood pressure when given mecamylamine (table 2). One patient (case 11) could not tolerate even minimum supine hypotensive doses of the drug because of fainting and totally disabling postural hypotension. Another patient (case 9), with advanced renal disease, developed bouts of severe diastolic hypertension after six weeks of an inadequate response; her blood pressure levels could not be controlled with daily doses of as much as 180 mg.

TABLE 1.—*Comparison of Daily Dose Requirement of Mecamylamine with Other Ganglionic Blocking Drugs*

	Prior Treatment				Mecamylamine Treatment	
			Dosage			
	Case No.	Medicament*	Av. Mg./Day	Variation, %	Av. Mg./Day	Variation, %
Responders	19	P(I.M.)	40	100	25	100
	20	P	400	100	30	83-133
	22	Ch+R	34	0-294	15	78-109
Nonresponders	29	Ch(I.M.)+R	2.8	71-143	44	68-136
	30	P+R	1,730	27-201	57	53-149
	31	P+R	60	100	10	0-150
	32	P+R	1,700	100	70	86-114
	33	C_6+R	1,815	55-165	15	0-200
	34	C_6+R	2,975	25-126	34	44-147
	35	C_6+R	2,428	62-113	68	88-110

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*P=pentolinium tartrate; Ch=chlorisondamine chloride; R=reserpine; C_6=hexamethonium. Unless indicated, drugs were given by mouth.

Eight of the 13 patients have maintained an average supine diastolic blood pressure of 110 mm. Hg or less during therapy for one to six months (average 3.8) and could be classed as satisfactory therapeutic responders. The pretreatment mean severity index of these responders was 9.3. The mean index fell to 5.6 during treatment; the supine diastolic pressure was reduced on the average by 21 mm. Hg (15%) and the standing diastolic on the average by 35 mm. Hg (28%). The average daily dose of the drug was 26 mg. The mean severity index was somewhat higher (10.9) before treatment among nonresponders than responders and was still quite elevated (8.7) when administration of the drug was discontinued. The average fall in supine diastolic pressure in this group was only 13 mm. Hg (9%). The average daily dose of the drug was 65 mg.

Administration of Mecamylamine to Previously Treated Patients.—In terms of its relative effect on supine diastolic pressure, mecamylamine was more effective than the previous antipressor treatments in 13 of 22 patients; it was no more effective in 2 patients and somewhat less effective in 7 (table 3).

Administration of mecamylamine was discontinued after one to two months of trial in five of these patients. In two of these it was ineffective. One (case 32) was a man with advanced cardiovascular and renal damage whose malignant hypertension had been brought under precarious and partial control during a year of treatment with pentolinium; while taking mecamylamine in doses up to 70 mg. daily, he developed bouts of hypertension (with supine diastolic pressures greater than 140 mm. Hg) and, on two occasions, pulmonary edema. The other patient (case 28) showed a significant rise (15 mm. Hg) in average supine diastolic pressure while taking mecamylamine and subsequently responded satisfactorily to a combination of hydralazine and reserpine. Mecamylamine therapy was discontinued in one patient (case 18) who had shown a good therapeutic response, because of intolerable dryness of the mouth, glossitis, and exacerbation of psoriasis. (Another patient, not in this study group, has also shown exacerbation of psoriasis while taking the drug.) One patient (case 29) stopped taking the drug because of a sensation of nervousness and anxiety and another (case 31) because of disabling postural hypotension.

Ten of the 22 patients have maintained an average supine diastolic blood pressure of less than 110 mm. Hg after continued therapy for 1 to 12 months (average 3.9) and are considered satisfactory responders to mecamylamine from the standpoint of the depressor effect of the drug. The pretreatment mean severity index of these responders was 7.1. The mean fell to 5.8 during treatment; the supine diastolic blood pressure was reduced on the average by 15 mm. Hg (13%). The average daily dose of the drug was 22 mg.

Mecamylamine therapy was continued in 12 patients whose average diastolic pressure was 110 mm. Hg or more during 1 to 12 months (average 2.7) of treatment. Only two of these nonresponders developed pressure averages significantly lower (12 and 24 mm. Hg) than they had shown during prior antihypertensive treatment with other ganglionic blocking agents or with

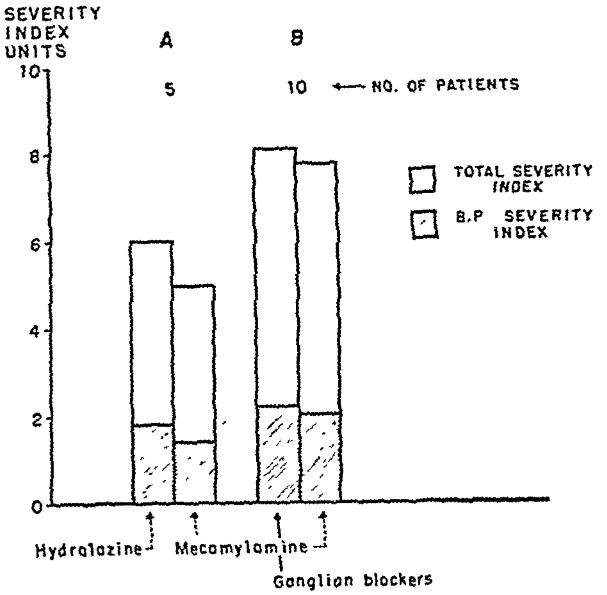
TABLE 2.—*Effect of Mecamylamine on Blood Pressure and Severity Index in Thirteen Hypertensive Patients Without Prior Treatment*

		Control		After Treatment				
						Supine Diastolic Blood Pressure, Av		
	Case No.	Total Severity Index	Supine Diastolic Blood Pressure, Av., Mm Hg	Daily Dose, Av., Mg.	Duration, Mo	Mm Hg	Decrease, Mm Hg	Total Severity Index
Responders	1	10.5	150	20.0	4.0	99	—51	6.5
	2	9.0	108	6.5	6.0	106	— 2	7.0
	3	5.0	108	35.0	3.5	107	— 1	3.0
	4	11.0	136	30.0	4.0	107	—29	6.0
	5	11.0	153	60.0	6.0	109	—44	7.0
	6	5.5	112	15.0	1.5	108	— 4	4.5
	7	8.5	119	15.0	3.0	106	—13	6.5
	8	11.0	135	30.0	2.0	110	—25	4.5
Nonresponders	9	12.0	149	180.0	1.5	146	— 3	10.5
	10	8.0	119	12.5	11.0	114	— 5	6.5
	11	12.0	158	80.0	1.0	124	—34	7.5
	12	10.5	125	35.0	2.0	114	—11	9.5
	13	12.0	140	15.0	1.8	112	—12	9.5

TABLE 3.—*Effect of Mecamylamine on Blood Pressure and Severity Index in Twenty-Two Patients with Prior Antihypertensive Treatment*

		Control		After Treatment				
						Supine Diastolic Blood Pressure, Av		
	Case No	Total Severity Index	Supine Diastolic Blood Pressure, Av., Mm Hg	Daily Dose, Av., Mg	Duration, Mo.	Mm Hg	Decrease, Mm Hg	Total Severity Index
Responders	14	6.5	122	27.5	12.0	98	—24	4.5
	15	6.0	121	35.0	1.0	109	—12	4.0
	16	7.0	110	20.0	2.0	85	—25	6.0
	17	7.0	114	5.0	3.0	101	—13	6.0
	18	6.0	110	40.0	2.0	85	—25	5.0
	19	8.0	99	25.0	3.0	105	+ 6	8.0
	20	10.0	134	30.0	1.5	110	—24	7.5
	21	3.0	108	15.0	3.0	102	— 6	3.0
	22	8.0	108	16.0	5.0	105	— 3	8.0
	23	9.5	118	10.0	7.0	93	—25	6.0
Nonresponders	24	7.5	111	37.5	12.0	114	+ 3	7.5
	25	8.5	113	25.0	4.0	112	— 1	6.0
	26	7.0	109	5.0	2.5	117	+ 8	8.0
	27	7.5	134	70.0	1.8	128	— 6	5.0
	28	7.0	106	180.0	1.0	121	+15	7.5
	29	6.5	123	44.0	1.0	139	+16	7.5
	30	6.0	111	57.0	2.0	111	...	6.0
	31	5.5	121	10.0	1.0	121	.	5.5
	32	9.0	132	70.0	1.0	120	—12	8.5
	33	6.0	107	15.0	1.0	114	+ 7	7.0
	34	12.0	141	34.0	2.5	117	—24	10.0
	35	10.0	126	68.0	1.0	133	+ 7	9.5

hydralazine. The mean severity index was 7.7 before the substitution of mecamylamine and was nearly the same (7.3) at the end of the study period. The average supine diastolic pressure in this group actually increased 1 mm. Hg (2%). The mean daily dose of the drug was 51 mg.



Changes in total severity index and blood pressure severity units observed in 15 patients with severe hypertension prior to and during one month of treatment with mecamylamine. Group A: prior treatment with hydralazine; group B: prior treatment with ganglionic blocking drugs. Single cross hatching indicates average supine diastolic pressure severity units.

Administration of Mecamylamine with Hydralazine.—Hydralazine (200 to 600 mg. daily) was added to the regimen of five patients (cases 36 through 40) who had been receiving mecamylamine alone for periods of one to two months. Only one patient had shown a good hypotensive response to the drug. The combination was used because the response to mecamylamine was inadequate and/or in the hope of diminishing side-effects by decreasing mecamylamine dosage. Improvement in control was obtained in three patients, in whom supine diastolic pressure was reduced by a mean of 18 mm. Hg, but a large reduction of mecamylamine dosage was possible in only one patient. One patient, who had shown a moderate response to mecamylamine alone, had no further effect from the addition of hydralazine, and the condition of one patient was resistant to both drugs, alone or in combination. The one patient whose mecamylamine dosage was substantially decreased experienced corresponding relief from its side-effects, but in the others the side-effects of hydralazine were merely added to those of mecamylamine.

Comparison of Mecamylamine Therapy with Previous Treatment.—Substitution of mecamylamine for hydralazine in five patients reduced the average supine diastolic pressures significantly in three, caused no appreciable change in one, and increased the average pressure in another (see figure). The over-all severity index in this small group was reduced from 6.0 to 4.9 after treatment for one month. Mecamylamine was substituted for another ganglionic blocking agent (hexamethonium, pentolinium tartrate, or chlorisondamine chloride) in 10 patients. After a month of therapy with mecamylamine, the average supine diastolic pressure in three had been reduced 15 mm. Hg or more (average 17 mm. Hg) below previous levels. The pressure averages remained approximately the same in five and were actually higher in two patients, so that there was no significant change in the average for the group. The total severity index averaged 8.1 before mecamylamine was given and was insignificantly changed (average 7.8) by its use for one month.

The observations do not show that mecamylamine is commonly much more effective in reducing diastolic hypertension than other ganglionic blocking agents. The observed improvement in depressor responses to mecamylamine was attributable more to the vigorous and meticulous control attainable by admitting the patient to the hospital than to the drug as such. All of the 10 patients had taken other ganglionic blocking drugs for a year or more, were skilled and confident in problems of self-medication, and had adjusted to their uncomfortable side-reactions. Five of them noticed little or no appreciable benefits of mecamylamine over the ganglionic blocking agent previously taken. Three patients definitely felt that blood pressure control was smoother and more predictable with mecamylamine and that side-effects, particularly constipation, were somewhat less severe. One patient (case 31) preferred pentolinium, stating that bouts of disabling orthostatic hypotension were less frequent; another patient (case 29) noted apprehension while taking mecamylamine and rejected it in favor of chlorisondamine, which had previously controlled her blood pressure.

Side-Effects

Of 35 patients, only one took mecamylamine in therapeutic doses without significant symptoms due to ganglion blockade. Of the 34 patients who had symptoms, 28 (80%) were uncomfortable but were able to continue the medication, while 6 (17%) were so disabled by side-effects that administration of the drug was discontinued. Symptoms usually persisted throughout the treatment period but were ordinarily either adequately controlled by other measures (bethanechol [Urecholine] chloride, laxatives, leg bandaging) or were finally tolerated without undue complaint. The character and incidence of these symptoms are given in detail in table 4. The severity of the side-effects was

Table 4.—*Severity and Nature of Side-Effects in Thirty-Five Hypertensive Patients Treated with Mecamylamine*

	Patients	
	No.	%
Degree of Severity		
No symptoms	1	3
Discomfort	28	80
Disabling	6	17
Nature		
Constipation	30	86
Blurring of vision	23	66
Dry mouth	22	63
Postural hypotension	22	63
Urinary retention	10	29
Nausea and vomiting	3	..
Impotence	3	..
Glossitis	2	..
Dysphagia	1	..
Fatigue	1	..

usually directly related to the amount of drug administered; tolerance to the hypotensive effect of mecamylamine with an increase in therapeutically effective dosage was almost invariably followed by an increase in symptoms. The side-effects in general resembled those observed during the use of other ganglionic blocking agents (hexamethonium, pentolinium, and chlorisondamine).

Gastrointestinal symptoms were most common and troublesome. Eighty-six per cent of the patients treated complained of constipation, but these patients responded to regular use of magnesium and/or emodin cathartics. Recurrent nausea and vomiting due to gastric atony occurred in three patients and was a factor in the discontinuance of medication in two of them. Patients were warned of the hazard of paralytic ileus, and this complication has been avoided in all patients by the early recognition and control of incipient intestinal paresis. Dryness of the mouth was commonly observed, occurring in 63% of patients, and was relieved, in part, by orally or sublingually administered bethanechol; dysphagia was a minor complaint of one patient and glossitis a disturbing problem in two.

Uncomfortable pupillary dilatation was noted to some degree by 66% of patients but was of major concern in only one; pilocarpine eye drops often gave some relief. Bladder atony with urinary retention was noted by half the male patients and could be controlled with administration of bethanechol in most, although one patient required transurethral prostatic resection. Impotence was not a frequent complaint in this group of patients, perhaps because sexual patterns had changed during previous therapy with other ganglionic blocking drugs; when directly questioned, all the males acknowledged its presence in some degree.

Disabling postural hypotension was a major factor in the discontinuance of therapy in four patients. Dizziness and faintness on standing was a common complaint in two-thirds of the group but became gradually less troublesome in most patients during the treatment period, responding to elastic bandaging of the legs, to adjustments in amount of drug given and changes in time of administration, and to the patient's learning to adapt to it.

Untoward Neuromuscular Complications

Five of the 35 patients in this study group and 2 others have shown signs of an unusual neuromuscular disorder during treatment with mecamylamine, although the manifestations in one (case 29) were subjective and the association with the drug uncertain. This complication has been manifested by mental symptoms, tremor, and convulsive seizures. These were observed in patients who presented evidences of diffuse, severe vascular disease, so that the abnormalities were at first attributed to cerebrovascular damage. In one patient, the symptoms were suppressed by anticonvulsant drugs, while mecamylamine therapy was continued; in four patients remission of symptoms tended to occur when mecamylamine therapy was discontinued. Similar manifestations had not been observed in patients of comparable physical status under treatment with other drugs, which suggested that this condition was an unusual complication of the use of mecamylamine in patients with severe hypertensive disease. (This conclusion gained support when we were informed by Dr. John R. Beem that like observations had been made by Drs. H. Mitchell Perry and Henry Schroeder at Barnes Hospital, St. Louis, in seven patients with malignant hypertension and uremia.) Relevant observations in our seven patients are tabulated (table 5) and are abstracted below.

Report of Cases

Case 32.—This 53-year-old man was noted above as exhibiting bouts of diastolic hypertension during mecamylamine treatment. These episodes were associated with a persistent state of intense anxiety and restlessness and with the development of a coarse jerking tremor increased by voluntary effort. Slight remission of symptoms occurred when intramuscularly given reserpine was substituted for mecamylamine; however, the patient died from cerebral hemorrhage one week later.

Case 20.—This 40-year-old engineer was given pentolinium and reserpine because of malignant hypertension with renal failure. Substitution of mecamylamine for pentolinium yielded an improved response in blood pressure, but, at the end of a month, he developed a "trembling feeling," for which he was given phenobarbital. Two months later the tremor had increased to the point where the patient was unable to write, and it was noted to be aggravated by emotion. The tremor involved all muscle groups and suggested to the neurological consultant a similarity to chronic (Huntington's) chorea. Symptoms did not subside by discontinuing reserpine therapy. The patient died at home of uremia some months later.

Table 5.—*Neuromuscular Complications Observed During Mecamylamine Therapy*

Case No	Duration Treatment, Mo	Dosage, Av Mg/Day	Blood Urea, Mg/100 Ml	Cerebrovascular Disease, Severity Index*	Presenting Symptoms
32	1.0	70	102	4.0(S)	Anxiety; mild tremor
20	1.5	30	81	1.5	Anxiety; marked tremor
4	5.0	30	45	1.0(E)	Anxiety; depression; convulsion; marked tremor
41	1.0	20	50	3.0(E)	Anxiety; convulsion; marked tremor
42	3.0	60	102	2.5(S)	Anxiety; depression; insomnia; dreams; moderate tremor
23	12.0	10	180	2.0	Marked tremor
29	1.0	44	27	3.0(E)(S)	Anxiety; mild tremor

* S = cerebrovascular accident; E = previous episodes of hypertensive encephalopathy.

Case 4.—This 43-year-old woman had malignant hypertension and was admitted with hypertensive encephalopathy and electrolyte imbalance, controlled by intravenously given sodium nitroprusside[7] and intramuscularly given hexamethonium. Mecamylamine was given for five months, with a favorable hypotensive response. At this time she developed increasing nervousness and depression and, by the sixth month of therapy, rapid, purposeless, irregular movements of the limbs, face, and body, increased by emotion and resembling ordinary (Sydenham's) chorea. Reserpine therapy had no apparent beneficial effect, and, shortly after admission to the hospital, she had two generalized convulsions. She was given diphenylhydantoin and phenobarbital in addition to reserpine and mecamylamine. She promptly improved and, at the end of one month, complained only of occasional jerky movements of the hands and some difficulty in writing.

Case 41.—This 39-year-old woman was admitted with malignant hypertension, mild ecephalopathy, and congestive heart failure, and, as emergency management, was placed on therapy with parenterally given reserpine and pentolinium. The glomerular filtration rate was 22 ml. per minute. A week later, she was given mecamylamine orally; hydralazine was added to the regimen two weeks later. On the fourth week of mecamylamine therapy she complained of "jitters," with involuntary jerking of the hands and arms, four days later, during which time nervousness increased, she had a grand mal seizure, for which she was given sodium phenobarbital intravenously. Subsequent neurological examination showed only a coarse tremor of the hands and tongue, which the neurological consultant could not associate with any known syndrome. Diphenylhydantoin was given, but the tremor increased and was not altered by discontinuing administration of reserpine or hydralazine. Two days after the convulsion, an electroencephalogram showed frequent paroxysms of slow waves and random spikes that were bilateral but not always synchronous on the two sides, the pattern was consistent with a convulsive disorder. An electromyographic record during the fourth week of the disorder indicated electrical silence of the muscle groups studied at rest, but, with voluntary effort, potentials appeared in an increasingly jerky, spasmodic fashion. This pattern was different from the normal sustained rise and also from the rhythmicity of most tremors, the record was suggestive of chorea or other extrapyramidal disease. Therapy with parenterally given pentolinium was substituted for mecamylamine therapy and was continued for three weeks, then discontinued, and small doses of mecamylamine (10 mg daily) were once again given. During the period of pentolinium therapy, the tremor and nervousness gradually diminished, but did not disappear, and increased slightly during two subsequent weeks on mecamylamine therapy.

Case 42.—This 54-year-old man has severe essential hypertension (remission of a former malignant phase having occurred during treatment), hypertensive heart disease, small residues of a recent stroke, and moderate renal failure. Control of the blood pressure with pentolinium and reserpine was only partial, so that administration of these was discontinued. Mecamylamine therapy slightly improved the blood pressure responses. However, three months later the patient complained of anxiety and depression, of insomnia, and of inappropriate and distasteful thoughts and dreams about his family and friends. He was increasingly aware of spontaneous jerking movements of the hands. On his admission to the hospital, an electroencephalogram showed regular, apparently normal rhythms. An electromyogram at rest showed spasmodic bursts of normal motor unit potentials, with long periods of electrical silence between them. With strong voluntary effort, potentials from the motor unit tested occurred as a sustained volley, but background disturbance appeared spasmodically, with intervening periods of electrical silence, the abnormal bursts occurred in no definable rhythm; the pattern was considered suggestive of chorea. One week after mecamylamine therapy was discontinued, the mental changes had all but disappeared and the tremor was greatly relieved. An electromyogram at this time showed sporadic involuntary bursts of potential that were less numerous than before.

Case 23.—This 63-year-old man had had remission of the malignant phase of hypertension, after treatment with hydralazine five years ago, and a state of severe essential hypertension has persisted since that time, with hypertensive renal (azotemia), cardiac and, presumably, cerebrovascular disease. During the past year his blood pressure has been satisfactorily controlled with small doses (10 mg daily average) of mecamylamine. However, at the end of one month of treatment he complained of intermittent dysphagia, which was most severe at the peak of the drug action. This was associated with slurring of speech. In the ninth month, the patient had a grand mal seizure, from which he promptly recovered and which has not recurred. The dysphagia, dysarthria, and the convulsion have been attributed to slowly progressive cerebrovascular damage. However, in the 12th month of treatment with mecamylamine he developed jerking, purposeless movements of the limbs and face, which increased over three weeks to the point where he found it difficult to write or eat. The effects on this of discontinuing mecamylamine therapy are under study.

Case 29.—This woman, aged 52, had severe essential hypertension accompanied by repeated attacks of convulsive hypertensive encephalopathy and, two years previously, by an apparent cerebral thrombosis. Her response to diphenylhydantoin and phenobarbital therapy and to ganglionic blocking agents was unsatisfactory. Urea clearance was about 40% of normal. Nine days after beginning treatment with mecamylamine she had another convulsion. This seizure was indistinguishable from her former convulsive attacks, the last of which had occurred three weeks before. Mecamylamine therapy was continued for another 40 days, during which time she complained of an intolerable feeling of fulness in the head, an indescribable apprehension and anxiety, and a mild tremor of the hands, all of which she associated with the drug. These complaints subsided promptly when chlorisondamine was substituted for mecamylamine, although convulsive attacks have recurred.

Comment

Effectiveness.—The primary aim of ganglion blockade in treatment of hypertensive disease is to effect decrease in arterial pressure, particularly the diastolic, which should be persistent throughout the 24 hours and present in the supine as well as the standing position. The average level of supine diastolic blood pressure is therefore used as the primary criterion of the effectiveness of mecamylamine and other antihypertensive drugs. By the criterion of supine diastolic pressure, accepting a level of less than 110 mm Hg as a satisfactory therapeutic response, mecamylamine orally is effective in about one-half of patients with severe hypertensive disease. All patients who were not receiving other ganglionic blocking drugs responded initially, those taking such drugs showed varying degrees of cross tolerance. Only about one patient in five was found to be, or became, so resistant to the action of mecamylamine as to show no decrease in average diastolic pressure. About one patient in three showed some depressor effect and, usually, temporary remission of signs of rapidly advancing vascular disease, but the level of control was, in general, inadequate. Our experience in this regard corresponds fairly well with that of previous observers, except that our percentages of favorable responses are less, presumably because our criteria of an adequate response are different.

Of greater interest than the absolute effectiveness of mecamylamine is the question of its effectiveness in comparison with similar agents. Mecamylamine had been adequately characterized pharmacologically as a potentially valuable ganglionic blocking agent before it was clinically evaluated. The most obvious distinction of the drug is that effective oral and parenteral doses are nearly the same, whereas those of other ganglionic blocking agents are widely different, the oral-parenteral effective dose ratio often being 10.1. As a result, especially in patients who can be classed as responders to mecamylamine, the average oral daily dose is small. Within limits, it is hardly significant whether a given dose is one of milligrams or grams. If it could be shown that the balance between absorption, excretion, and metabolism of mecamylamine were such that day to day variation in dosage was materially less than for other ganglionic blocking agents, then mecamylamine would have a distinct advantage. This, however, is not our experience. Irregularities in intestinal absorption are not, therefore, major factors in determining the variability of a patient's dosage requirement for a ganglionic blocking agent, since it is assumed that mecamylamine is completely absorbed, and the main determinant is seen to be variations in vascular responsiveness to the drug. Thus, what had been assumed to be a major advantage of mecamylamine is not fulfilled in practice. Nevertheless, some therapeutic advantage of mecamylamine remains, since effective oral and parenteral dosages are approximately equal.

Side-Effects.—The use of mecamylamine would also be clearly advantageous if it could be shown to elicit less of the extravascular effects of ganglion blockade than other agents of this sort. Unfortunately, this is not true. The side-effects correspond in all respects to those of other agents, except that possibly the large volume of distribution and relatively long duration of action of mecamylamine may tend to render some of them less intense during the first hours after taking the prescribed dose.

Neuromuscular Disorder.—The syndrome of jerky involuntary movements of muscle groups, particularly of the hands and arms, which suggested chorea to some observers and which was commonly accompanied by anxiety and also by bizarre mental aberrations in one or possibly two patients, and by convulsive seizures in two others, is described above. All these patients but one (case 29) were, or had been, in the malignant phase of hypertension; two had had strokes before, and one died from cerebral hemorrhage shortly after the syndrome became evident; three patients had experienced hypertensive encephalopathy. Thus, five of the seven patients had sustained hypertensive cerebrovascular damage that may have contributed to their susceptibility to this disorder. The association with renal failure is not as constant; only four of our seven patients showed noteworthy increases in blood urea concentrations, although all showed some evidences of renal damage, with rates of renal blood flow and glomerular filtration rate substantially less than normal. The one patient with a normal blood urea level is also the one (case 29) in whom the relation of the complaints to the drug is least convincing.

The degree of concern that may be attached to this complication is not entirely clear. The usual presenting symptoms of anxiety and tremor should not, at least in their initial phases, be particularly disturbing. However, the advance of these phenomena imposes a real disability, particularly when there are associated major convulsive seizures and disturbing mental changes. Consequently, it would seem advisable that patients taking mecamylamine be observed for involuntary choreiform movements and be questioned as to their psychic state, so that some other agent can be substituted for mecamylamine should such symptoms appear.

No explanation can yet be offered for this complication. The fact that mecamylamine is distributed in more than extracellular fluid volume suggests that it not only may act on the surfaces of the synapses, as do other ganglionic blocking drugs, but may diffuse into nerve cells as well. Indeed, the greater activity of mecamylamine than of other ganglionic blocking agents in inhibiting nicotine-induced convulsions is interpreted as evidence of a direct central nervous system action.[8] Such a localization of the drug might give rise to untoward phenomena, especially in the presence of focal cerebral ischemia and damage. Retrospectively, the syndrome recalled that of lithium intoxication in patients on low-sodium diets,[9] which was also associated with diffuse involuntary movements of skeletal muscle and, in some patients, with mental changes. The lithium syndrome differed, in that there was hyperreflexia and a tendency for fibrillary movements of skeletal muscles, both explained on the direct action of lithium on cell membranes of muscle and nerve. The mecamylamine syndrome is more suggestive of subcortical excitation. In principle, it would seem unlikely that such would be a direct action of the drug itself. Thus, the tremor described in toxicity tests of the drug is more probably attributable to neuromuscular block than to excitation. However, it is recalled that the drug is apparently metabolized in part and that its camphane nucleus may relate some of its possible metabolites to known excitatory agents. The accumulation of such products may be enhanced by renal damage and, in patients sensitized by cerebral vascular damage, might be a basic mechanism in this unusual complication.

Summary

Mecamylamine is a ganglionic blocking drug that has long duration of action and is apparently completely absorbed from the intestinal tract. It was effective in treatment in about one-half of a group of 35 patients with severe hypertensive disease, given average doses of about 25 mg. over periods of 1 to 12 months. In comparison with other ganglionic blocking agents, it is effective in smaller doses, is no more effective in reducing average blood pressure levels, and shows about the same variability of dosage from day to day. Side-effects are also similar, although possibly less intense during the first hours after a single oral dose. The therapeutic advantage is therefore small and lies mainly in the predictability of intestinal absorption.

Neuromuscular disorders were observed in seven patients taking this drug and took the form of anxiety associated with jerky, choreiform movements. Such symptoms may constitute a delayed, unusual toxic effect. Remission occurred in four patients, including one with definite mental aberrations and one who had convulsive seizures, when mecamylamine therapy was discontinued, and one patient responded to the use of anticonvulsive drugs. The symptoms in one patient were primarily subjective, and the association with use of the drug was less definite than in the other six. All these patients had sustained diffuse hypertensive cerebral and/or renal vascular damage, with azotemia present in four and strokes or encephalopathy as evidence of cerebral disease.

The possibility is suggested that some degradation product of mecamylamine may cause central nervous system excitation in such patients. It therefore seems desirable not to prolong the use of large doses of this drug in patients of this type and to observe them carefully for symptoms of this disorder, substituting another ganglionic blocking drug for mecamylamine as occasion arises.

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The mecamylamine and bethanechol chloride used in this study were supplied by Merck Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc., West Point, Pa.

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EFFECT OF CORTISONE IN ORCHITIS OF EPIDEMIC PAROTITIS (MUMPS)

Capt. George C. Risman (MC), U. S. Army

- *Epididymo-orchitis occurs in about 18 to 35% of cases of mumps. Orally given cortisone was used to treat five patients with this orchitis; 300 mg was administered for the first day, then at least 100 mg. a day for three days or more was used for maintenance, followed by the usual gradual withdrawal period. Significant symptomatic relief, evidenced by less pain and tenderness, occurred within 24 hours, but the duration of the infection and febrile response was apparently not shortened on the initially affected side. The subsequent contralateral orchitis, which occurred in three of the five cases, did appear milder and of shorter duration.*

Epidemic parotitis is a benign self-limited disease that attains clinical significance because of its high incidence and morbidity and the complications that frequently result, such as meningoencephalitis, pancreatitis, orchitis, and mastitis [1] The prophylactic and therapeutic treatment of orchitis and epididymo-orchitis has been the subject of many reports. Among the agents used have been chlortetracycline,[2] chloramphenicol,[3] oxytetracycline,[3a] diethylstilbestrol,[4] streptokinase,[5] convalescence serum,[6] and gamma globulin from pooled mumps convalescence serums.[6b] Except for gamma globulin from pooled mumps convalescence serums, none of these regimens have been generally accepted, nor have they been proved to be efficacious in either the prophylaxis or the treatment of orchitis. Recent reviews have adequately discussed the incidence and pathogenesis of orchitis and summarized the conflicting data of treatment.[7] Recent reports have suggested the efficacy of the steroid hormones in the treatment of orchitis.[8] In five of six cases observed by Solem,[9] the administration of 100 I. U. of corticotropin (ACTH) was thought to have resulted in dramatic relief of symptoms and signs.

This report presents five cases of orchitis secondary to mumps that were treated with cortisone. All five patients were soldiers and were treated in the hospital. Routine laboratory studies, consisting of a complete blood cell count, urinalysis, cardiolipin microflocculation test for syphilis, and roentgenogram of the chest, were within normal limits in all cases All patients were treated with complete bed rest except for bathroom privileges, a diet of choice, scrotal suspensory, and aspirin and barbiturate sedation as needed.

Report of Cases

CASE 1 —A male aged 42 years, was admitted to the hospital with bilateral parotitis of one day's duration Physical examination revealed bilateral parotitis of moderate degree and a temperature of 99 4 F (37.4 C) The serum amylase value was 63 5 mg per 100 cc (Somogyi). On the third hospital day, the patient's temperature rose to 100 F (37.7 C) and he complained of pain in the left testis The testis was swollen to about twice normal size and was dusky red in color and acutely tender. Cortisone was administered orally, 75 mg every six hours for four doses, and then dosage was maintained at 50 mg. every six hours for three additional days, after which the drug was gradually withdrawn (fig. 1). Within 24 hours the pain and swelling were both markedly reduced. On the fifth hospital day the right testis became swollen and patient complained of pain However, these symptoms were much less marked than those noted earlier. Despite marked symptomatic well-being, the patient's temperature spiked daily to 103 F (39 4 C) for four days, and profuse diaphoresis was noted On the ninth hospital day (the seventh day of orchitic symptoms), the temperature fell by crisis and remained normal Testicular swelling gradually subsided after administration of cortisone, but the testes did not return to normal size until the 10th hospital day (8th day after onset of symptoms).

In this case marked improvement in symptoms was noted after the administration of cortisone. An orchitis on the opposite side, however, developed 48 hours after treatment was started. There was no apparent effect on the duration nor on the degree of febrile response, and the resolution of orchitis was not significantly accelerated by cortisone.

CASE 2 —An 18-year-old male was admitted to the hospital with bilateral parotitis of one day's duration. Physical findings were normal except for enlarged parotid glands bilaterally. His temperature was 99 F (37 2 C). The patient's temperature was normal until the fifth hospital day, when it rose to 104 4 F (40 2 C), coincidental with mild swelling and severe pain in the left testis (fig 2). Cortisone was administered orally as follows 75 mg. every six hours for 4 doses, 50 mg. every six hours for 12 doses, and gradual withdrawal in the ensuing three days Within 24 hours there was significant diminution of pain, but little effect was shown on the fluctuating fever (fig 2) No significant effect on the testicular swelling was observed On the eighth hos-

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From the Medical Service, U S Army Hospital, Fort Jackson, S C

pital day, the right testis became slightly swollen and mildly painful. The signs and symptoms were less marked than those on the opposite side. Complete subsidence of swelling and pain bilaterally was noted on the 11th hospital day.

Considerable improvement of the local signs and symptoms was observed in this case after treatment was started, but complete resolution required six days.

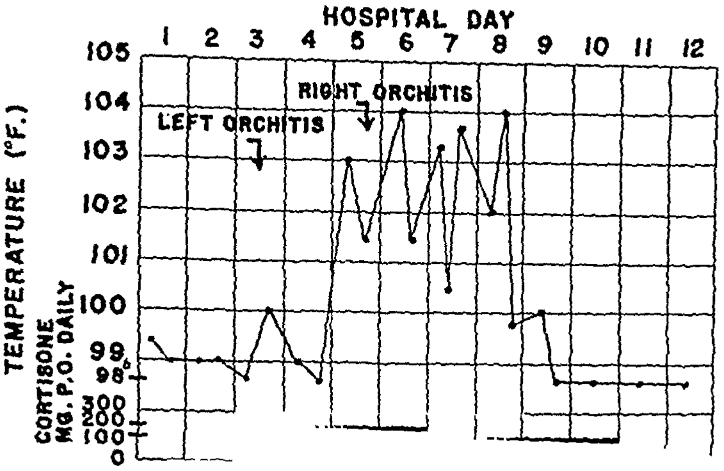

Fig. 1.—Chart of patient in case 1. Note the development of contralateral orchitis during cortisone therapy and the persistence of fever.

The fever was unaffected and persisted for four days. Three days after the onset of therapy, orchitis that was of mild degree developed in the opposite testis and lasted four days.

CASE 3.—A male, aged 20, was admitted to the hospital with parotitis on the right of one day's duration. Physical examination was normal except for finding of enlargement of the right parotid gland to about twice normal size. On the sixth hospital night the patient's temperature rose to 100 F and he complained of pain in the left testis. On the following day the patient's temperature was 102 F (38.8 C) and the testis was enlarged, red, hot, and acutely tender. Cortisone was administered orally as follows: 75 mg. every six hours for four doses, 50 mg. every eight hours for three doses, 75 mg. every eight hours for four days, and gradual withdrawal in the ensuing three days. A mild reduction in swelling and marked decrease in pain were noted in 24 hours. His temperature continued to spike to 102 F daily (fig. 3). On the 10th hospital day the right testis became swollen and painful. At this time the patient was receiving 225 mg. of cortisone daily. The left testis returned to normal size after seven days, while the right testis became free of swelling five days after onset of symptoms.

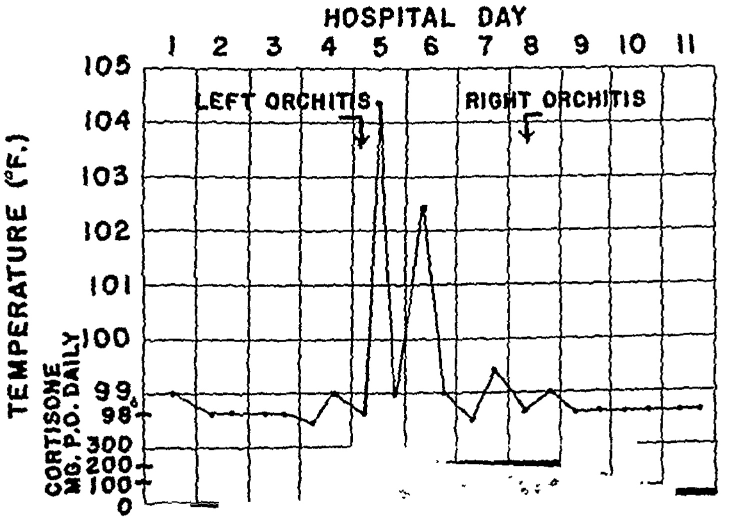

Fig. 2.—Chart of patient in case 2, showing fluctuating course of fever during administration of cortisone.

A significant symptomatic response to cortisone occurred in this case. However, neither the fever nor the testicular swelling was significantly affected. Cortisone did not prevent the appearance of contralateral orchitis but appeared to ameliorate the severity of its symptoms.

CASE 4.—A 21-year-old male was admitted to the hospital with bilateral parotitis of one day's duration. Physical examination was otherwise normal. The patient's temperature was 99.5 F (37.5 C). The serum amylase level was 112 mg. per 100 cc. (Somogyi). A single temperature elevation to 104 F occurred on the second hospital day, but no abnormal findings were noted. On the fifth hospital day his temperature rose to 103.5 F (39.7 C) and bilateral orchitis was noted. Cortisone was administered as follows: 75 mg. every six hours for four doses, 50 mg. every six hours for four doses, and 25 mg. every six hours for the following two days. Symptomatic response was excellent, but persistence of slight testicular swelling was noted bilaterally. On the 10th hospital day, while cortisone was still being administered, the right testis increased in size and became more painful, coincidental with a rise in temperature. Dosage was increased to 75 mg. every six hours. A remission of signs and symptoms was noted on the next day, after which cortisone was gradually withdrawn. Both testes became normal in size on the 12th hospital day, and fever fell by lysis on the 13th day.

The symptomatic response to cortisone in this case was comparable to that in preceding cases. However, a relapse of fever and an increase in testicular swelling and pain occurred while the patient was receiving 100 mg. of cortisone daily. A remission of symptoms appeared to be related to an increase in dosage.

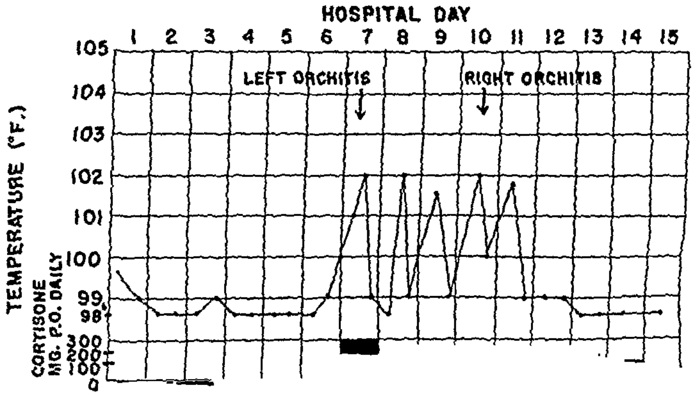

Fig. 3.—Chart of patient in case 3, showing occurrence of contralateral orchitis four days after cortisone therapy was begun.

CASE 5.—A 28-year-old male was admitted to the hospital with known exposure to mumps and parotitis on the left of one day's duration. On physical examination, findings were normal, except for the enlargement of the left parotid gland and a temperature of 99.5 F. On the third hospital day the right parotid gland became enlarged and the patient's temperature rose to 101 F (38.3 C). On the fifth hospital day orchitis developed on the right. Every six hours, 75 mg. of cortisone was given, and this dosage was continued for the next three days (fig. 4). Symptomatic improvement resulted, although no significant resolution of testicular swelling was noted. On the sixth hospital day the testis was more swollen, tense, and turgid but less painful. Fever continued, with daily elevations of the temperature to 103 F, but fell by crisis on the eighth hospital day. The testicular swelling gradually subsided during the ensuing four days. Withdrawal of cortisone was begun on the 8th hospital day and completed on the 12th hospital day. Loss of normal turgor and some softening were noted on the 11th hospital day.

Within 24 hours after cortisone was given, significant, but incomplete, relief of pain was observed in this case. Fever persisted for four days and testicular swelling persisted for six days, despite large doses of the steroid.

Comment

The incidence of epididymo-orchitis as a complication of epidemic parotitis has ranged from 18 to 35% in different series.[10] While testicular atrophy occurs in 35 to 50% of the patients, the occurrence of sterility is thought to be low.[1d] The multiple therapeutic agents used in the treatment of orchitis attest to the failure of any one to be significantly effective. No prophylactic therapy except gamma globulin from mumps convalescence serums has been found effective in reducing the incidence of orchitis.[6b] The administration of estrogenic substances in various doses has not reduced the incidence of orchitis, although Hoyne and co-workers [4a] reported its efficacy. In their report, seven patients given 2 mg. of diethylstilbestrol three times a day did not develop orchitis. However, the small size of the series and the inherent variability of the disease vitiate any conclusions. Other reports[11] including larger number of patients have not confirmed these observations. Therapeutically, however, estrogenic substances have been found to ameliorate the severity of symptoms in many cases.[4] Various antibiotics, such as chlortetracycline and chloramphenicol, have also been used, with dubious and inconsistent results.[12]

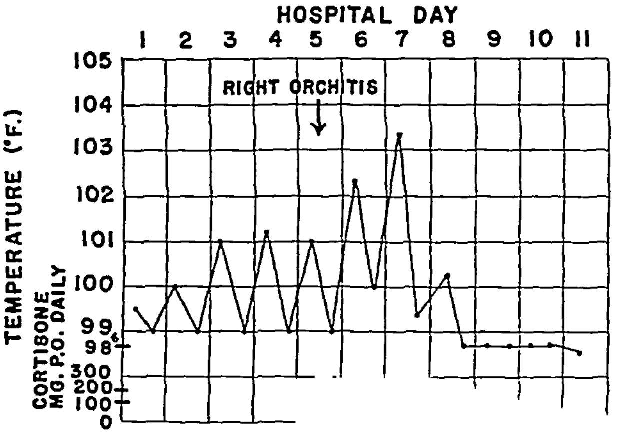

Fig. 4.—Chart of patient in case 5, showing febrile course while on cortisone therapy.

No reports on the prophylactic use of the steroid hormones or the adrenocorticotropic hormone are known to me. However, several statements of their therapeutic effectiveness in symptomatic treatment are available.[8] Solem [9] noted the dramatic subsidence of acute inflammation and swelling within 24 hours after administration of 100 I. U. of adrenocorticotropic hormone in five of six cases. In these instances, however, corticotropin was not administered until the third or fourth day after the onset of orchitis. The possibility of a normal resolution unaffected by therapy occurring four days after onset of symptoms must be considered. In one case a relapse occurred that responded to a second dose of corticotropin on the sixth day.

The use of cortisone in my experience did not afford as salutary or dramatic relief as the previous use of corticotropin had indicated. In the five cases presented, significant, but incomplete, relief was obtained within 24 hours. While the severity of symptoms was markedly reduced, no effect on the duration or degree of fever was noted. The pathogenesis of the infection also was not affected, varying from five to eight days. Three patients developed contralateral orchitis while receiving 100 mg. or more of cortisone daily. In these cases the duration and severity of the contralateral orchitis appeared to be ameliorated. It is apparent that the use of cortisone is indicated only for subjective relief and that it does not affect the course of the disease.

Summary and Conclusions

Five patients with orchitis secondary to epidemic parotitis (mumps) were treated with cortisone. Treatment varied but in all cases was commenced with 300 mg. given orally on the first day symptoms were observed and was maintained with 100 mg. or more daily. Significant amelioration of pain and tenderness occurred within 24 hours, but the duration of swelling was unaffected. Cortisone neither shortened the course of ipsilateral orchitis nor affected the degree of febrile response. Cortisone did not prevent the occurrence of an orchitis on the opposite side, which developed in three patients while they were taking large doses. Symptoms in the contralateral testis were milder, and the duration of inflammation was shorter. No adverse sequelae attributable to cortisone were noted during or following this short-term period of therapy. The course of parotitis did not appear affected by the administration of the hormone. Cortisone can be added to the therapeutic armamentarium for orchitis of epidemic parotitis. Its usage, however, provides only symptomatic relief. All the attendant risks of steroid therapy must be borne in mind during its administration.

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INFLUENCE OF HEART DISEASE ON SURGICAL RISK

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• *The risk involved in surgical operations on patients with heart disease was studied in 101 patients undergoing 134 operations, and the results were compared with those from a series of 69 surgical patients free from heart disease. The mean ages of the two groups were 61 and 49 years respectively. The gross mortality rates in the two groups were 7.4% and 1.4%, and the rates of incidence of cardiovascular and respiratory complications were 21.6% and 5.6% respectively. The risk for the cardiac patient was therefore greater, but it was not excessive. Patients having an abnormal electrocardiogram as the only cardiac finding and those having hypertensive heart disease or a combination of hypertensive and arteriosclerotic heart disease had no cardiac deaths and suffered no cardiorespiratory complications, but patients with anginal syndrome had a 7% cardiac death rate and a 35% incidence of cardiorespiratory complications. The history is of prime importance in determining the magnitude of the risk, and careful attention to preoperative care, surgical and anesthetic technique, and postoperative care is needed.*

For many years, the impression prevailed among physicians that the presence of organic heart disease increased to a considerable degree the risk in patients undergoing surgery. Within the recent past, several contributions to the medical literature have served to dispel this impression. Proger[1] in 1955 reported on the results in some 500 patients with arteriosclerotic heart disease undergoing major surgery and found a mortality rate of approximately 1%. This compared favorably with the mortality rate in patients without heart disease undergoing comparable surgical procedures. In a more recent review of the problem of surgical risk, Moyer and Key[2] stated that, as more surgical experience is gained with patients having pulmonary or cardiac diseases, these diseases have become less important as determinants of operative risk. Several years ago we undertook this clinical study to help us judge the accuracy of the decisions of the internists in our own hospital regarding operative risk in patients with heart disease. In an aging population such as one finds in a veterans hospital, this is a problem of great magnitude.

Material and Methods

The patients studied were those in our hospital (all male veterans) known to have had heart disease who were subjected to major surgery from January, 1950, through February, 1955. The patients ranged in age from 23 to 85 years, with an average age of 60.9 years. There were 101 patients who underwent a total of 134 operative procedures. In the first 30 days, there were 10 deaths, 3 of them cardiac, and 29 cardiorespiratory complications. The most common surgical procedure in this series was repair of inguinal hernia, carried out 22 times. There were, in addition, 15 transurethral prostatic resections, 14 lumbar sympathectomies, 12 leg amputations, and 8 each of cholecystectomies, suprapubic prostatectomies, and subtotal gastrectomies. The remainder constituted a variety of surgical procedures. Table 1 shows the etiological types of heart disease encountered and the groups in which postoperative deaths occurred. There were 72 patients who had arteriosclerotic heart disease alone or in combination with other etiological types. The majority of the remaining patients had either hypertensive or rheumatic heart disease.

Anesthesia.—The relation of anesthesia to the postoperative mortality and postoperative course is of interest. In this series, spinal anesthetics were used in 68% of the operations. It is considered that the use of spinal anesthesia may have contributed to the death of two patients in this series. A third death was due to laryngospasm occurring during spinal anesthesia. The use of spinal anesthetics in patients with coronary disease has been the subject of a separate study, to be reported elsewhere.[3]

Mortality and Complications

In 134 operative procedures, there were 10 deaths within the first 30 postoperative days, an over-all mortality rate of 7.4%. Three of these deaths were considered to be cardiac, a cardiac death rate of 2.2%. Cardiac deaths followed a cervical sympathectomy, a leg amputation, and exploratory laparotomy. Table 1 shows the types of heart disease from which the patients who died suffered. Brief reports on the patients considered to have suffered cardiac deaths follow:

Case 1.—A 53-year-old male with rheumatic and arteriosclerotic heart disease with aortic stenosis and insufficiency, atrial fibrillation, and a history of congestive heart failure was admitted because of cardiac decompensation. Emergency popliteal embolectomy was followed by gangrene of the involved extremity, requiring a midthigh amputation. Four days after amputation the patient died suddenly and was found to have a posterior myocardial infarction about four days old.

Case 2.—A 71-year-old male who suffered a myocardial infarction six hours preoperatively underwent an exploratory laparotomy for fresh mesenteric artery occlusion. Shortly after induction of spinal anesthesia there was a sudden and precipitous fall in blood pressure, and the patient died within 12 hours. At autopsy there was evidence of recent myocardial infarction.

Case 3.—A 61-year-old male died suddenly three days after cervical sympathectomy carried out for intractable anginal syndrome. An electrocardiogram provided evidence of postoperative posterior myocardial infarction.

From the Veterans Administration Center.

Read before the Ninth Clinical Meeting of the American Medical Association, Boston, Nov. 30, 1955.

Deaths considered noncardiac in this series were due to carcinomatosis, overwhelming infection, bronchogenic carcinoma, electrolyte imbalance, laryngospasm, cerebral vascular accident, and generalized peritonitis.

With all complications occurring during the first 30 postoperative days considered, 84 (63%) of the operations were not followed by complications. Twenty-nine (21.6%) were followed by cardiovascular or respiratory complications and 20 (15%) by surgical complications only. Table 2 lists the cardiovascular and respiratory complications and the complications that were considered to be of surgical origin and unrelated to heart disease. Certain of the patients suffered more than one complication.

"Risk Rate"

As there were in our series only 13 instances of rheumatic heart disease uncomplicated by coronary disease, we have used the figures of Morrison[4] along with our own figures for the two major types of heart disease encountered in this series (table 3). We had 72 patients with arteriosclerotic heart disease alone or in combination with other types undergoing 96 operative procedures, with 10 deaths from all causes, a death rate of 10.4% and a complication rate of 24%. We have used the term "risk rate," coined by Morrison, which is the sum of the death rate and the complication rate. The risk rate in our patients with arteriosclerotic heart disease, including those with conditions having combined etiologies, was 34%. The figures of the hypertensive group are of interest, in that there were 13 patients undergoing 21 operations, with no deaths and no complications.

TABLE 1.—*Etiological Types of Heart Disease*

	Patients, No.	Deaths, No.
Arteriosclerotic	61	
Old infarctions	26	5
Fresh infarctions	4	2*
Anginal syndrome only	14	1†
Abnormal electrocardiogram	11	2
Congestive failure only	6	
Arteriosclerotic, with arterial hypertension	7	
Hypertensive	13	
Syphilitic	1	
Calcific aortic stenosis	9	
Rheumatic	4	
Rheumatic and arteriosclerotic	3	
Atrial fibrillation	2	
Pericarditis, constrictive	1	

* Both due to heart disease.
† Due to heart disease.

Controls.—For comparison, a series of 69 consecutive patients without heart disease undergoing similar operations was studied from the point of view of mortality and cardiovascular or respiratory complications. Ages ranged from 29 to 82, averaging 49 years. In this group, there were no cardiac deaths and there was a single noncardiac death (1.4%). There were four cardiovascular or respiratory complications (5.6%): one case each of atelectasis and thrombophlebitis occurring in patients undergoing repair of inguinal hernia, one case of thrombophlebitis in a patient who had undergone a suprapubic prostatectomy, and one pulmonary infarction in a patient who had had a subtotal gastrectomy.

Risk Rate According to Type of Heart Disease.—In an attempt to evaluate the prognostic significance of several of the more common manifestations and etiological types of heart disease, the mortality and complication rates in these groups were studied. It is to be noted that several patients have been included in more than one of the following categories. There were 19 patients with a history of congestive heart failure, all compensated at time of operation, and they underwent 26 operative procedures. The majority of these patients had arteriosclerotic heart disease. No complications followed 18 of the procedures. There was one cardiac death, and there were seven cardiovascular or respiratory complications, which included one case each of coronary insufficiency, myocardial infarction, pulmonary edema, atelectasis, and pneumonia. There were two cases of pulmonary infarction.

TABLE 2.—*Complications Occurring in the First 30 Days After 134 Operations*

	No.
Cardiorespiratory	
Myocardial infarction	8
Coronary insufficiency	6
Congestive failure	3
Arrhythmia	1
Cerebral vascular accident	1
Dyspnea	2
Pulmonary infarction	6
Pneumonia	2
Atelectasis	3
Thrombophlebitis	2
Surgical	
Genitourinary bleeding	5
Fever of undetermined origin	4
Electrolyte imbalance	2
Shock	4
Gastrointestinal bleeding	1
Peritonitis	1
Jaundice	1
Abdominal pain of unknown cause	1
Distention	1
Oliguria	1
Laryngospasm	1
Rash	1
Wound disruption	2

Twenty-six patients who had had old myocardial infarctions underwent a total of 38 operative procedures. There were four deaths, all of which were noncardiac. Twenty-six of the operative procedures were uncomplicated. There were 12 cardiovascular or respiratory complications in the remaining patients, including one each of atrial fibrillation, postoperative dyspnea of unknown cause, atelectasis, and cerebral vascular accident and two cases of coronary insufficiency, two of pneumonia, and four of pulmonary infarction. There were five patients with myocardial infarctions that had occurred less than six weeks preoperatively. These patients underwent a total of five

TABLE 3.—*Deaths and Complications According to Etiology of Heart Disease in the Present Series and in Morrison's Series*

	Present Series		Morrison*	
	Arteriosclerotic	Hypertensive	Rheumatic	Arteriosclerotic
Patients, no.	72	13	150	311
Operations, no.	96	21	159	485
Deaths, no.	10	0	7	72
Death rate, %	10.4	0	3.7	14.8
Complication rate, %	24.0	0	3.7	4.3
Risk rate, %	34.4	0	7.4	19.1

* Data from Morrison.[4]

operative procedures, and in this group two deaths resulted, both of which were considered to be cardiac deaths. The course of two of the three surviving patients was complicated by coronary insufficiency.

There were 28 patients with a history of anginal syndrome or coronary insufficiency who underwent a total of 37 operative procedures, which resulted in six postoperative deaths, two of which were cardiac. Twenty-three of the operations were not followed by cardiovascular or respiratory complications. There were 13 of these complications in the remaining patients, including one each of pulmonary edema, atrial fibrillation, atelectasis, and postoperative dyspnea of unknown cause. There were, in addition, four myocardial infarctions, two cases of coronary insufficiency, and three cases of pulmonary infarction. There were 10 patients with asymptomatic arteriosclerotic heart disease diagnosed by electrocardiogram only who were subjected to a total of 10 operative procedures. The only death was noncardiac, and there were no cardiovascular or respiratory complications.

Eight patients with arterial hypertension and arteriosclerotic heart disease withstood 11 operative procedures with no mortality and no cardiovascular or respiratory complications. Although this group is too small for these findings to be of statistical significance, it is of interest that Morrison, in a larger group, also found that patients with arteriosclerotic heart disease in combination with hypertension did considerably better than patients with arteriosclerotic heart disease and a normal blood pressure. The significance of these findings is not apparent to us at this time. Six patients with rheumatic and arteriosclerotic heart disease underwent a total of seven operations. There was one cardiac death, and there were three cardiovascular or respiratory complications, which included one case each of myocardial infarction, pulmonary edema, and atelectasis.

Comment

On the basis of this study it is concluded that operative risk in patients with heart disease is not excessive. However, the cardiovascular and respiratory complication rate is considerably higher than in noncardiac patients undergoing comparable surgical procedures. In evaluating cardiac patients for surgery, history is of prime importance in helping to determine whether or not a patient is a good operative risk. The presence of dyspnea or anginal syndrome on exertion and the degree of exertion necessary to produce these symptoms are probably of greater importance than information provided by physical examination or the electrocardiogram. Preoperative preparation of these patients warrants most careful attention. Of particular importance is the correction of anemia and the institution of measures aimed at restoring the status of cardiac compensation. If atrial fibrillation exists, preoperative digitalization aimed at controlling the ventricular rate is certainly indicated.

The best available surgical and anesthetic techniques are required in order that anoxia, shock, and wide fluctuations in blood pressure may be avoided. Fluid requirements should be carefully determined both during and after surgery so that overloading of the circulation, particularly with sodium-containing fluids, is avoided. Results in this study indicate that these patients are especially susceptible to cardiovascular and respiratory complications, the commonest of which are atelectasis, thromboembolic disease, and postoperative coronary insufficiency. Superior nursing care aimed particularly at eliminating the retention of tracheobronchial secretions and the development of venous thrombosis, as well as frequent careful observation by the physician to insure early detection and treatment of this complication, is mandatory. The liberal use of oxygen therapy and bronchodilators may be of great benefit.

Summary

One hundred one cardiac patients underwent 134 major surgical procedures. The gross mortality rate from all causes was 7.4%, and the mortality rate directly attributable to heart disease was 2.2%. The incidence of cardiovascular and respiratory complications was 21.6%. In a control series of noncardiac patients the mortality rate was 1.4% and the cardiorespiratory complication rate 5.6%. The largest group of patients, those with arteriosclerotic heart disease, had a 3% incidence of cardiac deaths and a surprisingly high rate of nonfatal cardiorespiratory complications (24%). Two out of five patients with fresh myocardial infarctions at the time of operation died, and there were two cardiorespiratory complications in the three survivors. Patients with anginal syndrome had a 7% cardiac death rate and a 35% incidence of cardiorespiratory complications. Patients with old myocardial infarctions had no cardiac mortality but a 31% incidence of cardiorespiratory complications. Patients with a history of congestive heart failure had a 3% cardiac death rate and a 27% cardiorespiratory complication rate. Patients having an abnormal electrocardiogram as the only cardiac finding and those having hypertensive heart disease or a combination of hypertensive and arteriosclerotic heart disease had no cardiac deaths and suffered no cardiorespiratory complications. In view of the increased susceptibility of these patients to cardiovascular and respiratory complications, there is a need for the best of preoperative and postoperative care and careful attention to the details of surgical and anesthetic techniques.

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Urinary Calculi.—The diagnosis of urinary lithiasis does not end the physician's diagnostic responsibility. It is incumbent upon him to determine if a metabolic disease has contributed to the formation of the stone. . . . A high index of suspicion, plus a systematic investigation by means of a specific history, urine straining, examination of the calculus, roentgenogram of the abdomen, and appropriate blood studies, may be rewarded by the uncovering of a metabolic defect.— R. P. Spencer, Metabolic Diseases and Urinary Calculi, *United States Armed Forces Medical Journal*, August, 1956.

TYPHOID-PARATYPHOID VACCINE WITH CHLORAMPHENICOL IN RECURRENCES OF SALMONELLOSIS

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• *Salmonellosis in 86 patients was treated with chloramphenicol and typhoid-paratyphoid vaccine. The chloramphenicol caused the temperature to return to normal generally within four days. The frequency of recurrences depended on the amount of vaccine given. The ratios for recurrence were 1:4 (i. e., 4 out of 16) for patients treated without vaccine, 1:7 in 29 patients treated with less than 1.5 cc. of vaccine, and 1:20 in 41 patients treated with more than 1.5 cc. of vaccine. The combined therapy appeared to be a promising means of reducing the danger of recurrence.*

This is a preliminary report of studies still in progress on the use of typhoid-paratyphoid vaccine administered with chloramphenicol in an attempt to prevent recurrences of Salmonella infections. Due to limited facilities and an overwhelming number of patients, the studies on these cases are not extensive. Furthermore, we have no inpatient service and the home visiting program cannot follow up patients as closely as desired. However, we hope this report may stimulate further studies in centers better equipped to evaluate such work.

Methods and Material

During the three months of October, November, and December, 1955, in our clinic, 74 blood cultures and 377 stool cultures were found to be positive for Salmonella organisms. In addition, there were many reports of Aerobacter that may have been from stools containing Salmonella. In our small laboratory, it is impossible to isolate every colony on a stool culture, and a colony of Aerobacter may be chosen and one of Salmonella organisms left, since they are grossly indistinguishable. Clinically active infection occurred in, and sufficient data are available on, 48 patients with positive blood cultures and 36 with positive stool cultures. We have included also two patients whose culture reports were of Aerobacter but whose clinical indications of infection and Widal agglutination tests gave us no reason to doubt the origin of the infection. This gives a total of 86 patients.

During the early part of the study, blood cultures were made only on those patients whose urine showed a positive Ehrlich diazo reaction. Otherwise a stool culture alone was done. This method has proved unsatisfactory for screening, as some with negative Ehrlich diazo reactions have positive blood cultures and vice versa. At present, we have blood culture, stool culture, and Widal agglutination tests made when the clinical diagnosis is positive.

The mode of administration of chloramphenicol was oral except for an initial parenteral dose in several of the most seriously ill patients. Dosage was 500 mg. every six hours (2 gm. daily), except in a very few patients who received 500 mg. every four hours for the first day or two. The dosage for the children ranged from 30 to 50 mg. per kilogram of body weight for 24 hours. At the same time we gave typhoid-paratyphoid vaccine, 0.1 or 0.2 cc. daily. (Each cubic centimeter of vaccine contained 1 billion Salmonella typhosa organisms, 250 million S. paratyphi A, and 250 million S. paratyphi B.) The chloramphenicol dosage we found satisfactory, as fever had decreased, if it was not absent, by the end of four days, and it seemed to continue to decrease even if the drug was withdrawn. In only one case was it found necessary to give a second course of chloramphenicol because the fever failed to decrease several days after the cessation of therapy. The dosage of typhoid-paratyphoid vaccine, on the other hand, proved to be inadequate. It was therefore increased to 0.3 cc., 0.4 cc., and 0.5 cc. on successive days, and then 0.5 cc. was given three times weekly for at least a month in adults. The patients may have a soreness at the site of injection and a mild rise in fever a few hours after the injection, which may be controlled with the administration of acetylsalicylic acid. In no case was it necessary to stop therapy. The intravenous route was not employed.

Of the 86 patients included in this study, 45 were males and 41 females. The ages ranged from 8 months to 46 years. One patient was under one year of age, 21 were in the first decade, 34 were in the second decade, 9 were in the third decade, and 8 were in the fourth decade. In 23 patients blood cultures were positive for Salmonella typhosa, in 23 for S. choleraesuis, in one for both these organisms, and in one for an as yet unidentified organism of the S. paratyphi C group. Stool cultures on admission showed S. typhosa in 7, S. choleraesuis in 24, S. paratyphi A in 3, and S. typhimurium in 2. As mentioned above, two patients had clinically typical Salmonella infections, with high-titer Widal agglutinations for typhoid in one and for S. choleraesuis in the other, despite a report of only Aerobacter organisms in the stool culture.

Length of time since onset of symptoms varied in the patients with positive stool cultures. Twenty-two were tested in the first week, 11 in the second week, 7 in the third week, 8 in the fourth week, and 2 in the fifth week. No time was recorded for one. There were two patients in whom only the Widal reaction was used for confirmation. The length of time since the onset was two weeks in the patient with a culture showing S. choleraesuis, and in a patient with a culture showing S. typhosa there had been a recurrence.

From the Maryknoll Sisters Clinic.

Results

There were recurrences in 17 patients, of whom 7 gave a history on admission of previous illness, a latent period, and recurrence; while 10 had had recurrences after receiving treatment at our clinic. The length of time from initial onset to recurrence varied from 2 to 11 weeks, while that from the end of treatment with antibiotics to reappearance of symptoms was six days to 6 weeks. However, all recurrences occurred within three weeks, except in one case, in which the recurrence occurred at six weeks. It is possible that this was a new infection with another member of the Salmonella family rather than a real recurrence. Six of the patients who were admitted with recurrences had received no previous antibiotic therapy and had had latent periods of 2 to 10 days, having been back at work or school after long illness when the symptoms reappeared. The other patient with a recurrence had taken chlortetracycline, had been well for a week, and then had relapsed. Of those relapsing after treatment at our clinic, nine were treated with chloramphenicol, one with tetracycline, and one with a combination of these drugs.

As we felt that the therapy with vaccine and antibiotics was of definite value, and since there are many reports on the recurrence rate of Salmonella infections, we soon abandoned the plan of giving vaccine to only alternate patients. Furthermore, with the high incidence of salmonellosis, we did not think it necessary to use only antibiotic therapy when a recurrence might be prevented. In this way we have been able to treat a larger number of patients successfully. We thus decided to continue the study only to ascertain the degree of effectiveness of vaccine, the ideal dosage, and a desirable period of administration.

On these cases, however, we do have a few statistics that seem divergent enough to be of value. In 86 patients treated with antibiotics, we had 10 patients with recurrences while under observation. The recurrences were apparently unrelated to the type of Salmonella infecting, as the types of Salmonella were fairly evenly represented. However, there was an interesting correlation with the vaccine therapy. In 16 cases treated without vaccine, there were four recurrences; in 29 cases treated with less than 1.5 cc. of vaccine, there were four recurrences; and in 41 cases treated with over 1.5 cc. of vaccine, there were two recurrences. One of the two patients in the last group received 1.7 cc. and the other 2.1 cc. of the vaccine. The latter was a 3-year-old child in whom the recurrence was diagnosed clinically only. It may have been another concurrent infection, but the case was included here as possibly one of recurrence despite vaccine therapy. This gives ratios for recurrence of 1:4 in patients treated without vaccine, 1:7 in those given less than 1.5 cc. of vaccine, and 1:20 in those receiving over 1.5 cc. This would seem to prove at least that this work is worthy of further investigation.

The chloramphenicol used in this study was supplied as Chloromycetin by Parke, Davis & Company, Detroit.

CLINICAL NOTES

FATAL URETHAN POISONING AFTER TOPICAL THERAPY WITH URETHAN

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and
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Urethan (ethyl carbamate) has been used as an anesthetic agent in experimental animals for many years. It has the advantage of producing satisfactory anesthesia without respiratory depression. This property has been put to use in obstetrics.[1] Observations of its effect on the hemopoietic system and mitotic cells has led to its use in the treatment of leukemia[2] and other malignant diseases.[3] The cytotoxic action of urethan can be responsible for renal and hepatic damage in addition to bone-marrow depression and sedation. Nausea, vomiting, and anorexia are undesirable side-effects. Reports by Weinstein[4] and Howe.[5] on bacteriostatic action indicate its value in the treatment of wounds and burns. Howe,[6] reporting on the toxic effects of topically applied urethan in 67 patients, found no hematological changes or evidence of liver damage. The amounts used ranged from 30 to 600 cc. of 10% solution daily for 2 to 19 days. One patient received 755 cc. of 10% solution daily for 10 days. In a group of histories added to the original report, he cited a case of a 66-year-old woman who became drowsy, disoriented, and nauseated and who vomited after 200 cc. of 5% solution had been used hourly for 24 hours in bladder irrigations. The symptoms cleared within 24 hours after the drug was withdrawn. Two other instances of anemia and leukopenia, one fatal, the other temporary, were also added to the original report. This case report illustrates the possibility of absorption of fatal amounts of the drug when it is used topically. The initial symptoms were profound general anesthesia and vomiting. Within a few days, bone-marrow depression became evident, and the patient succumbed to massive hemorrhage.

Report of a Case

A 21-year-old male was admitted to the West Haven Veterans Administration hospital on Jan. 11, 1955, for the treatment of burns. Two days prior to his admission he sustained first and second degree burns of the upper extremities, anterior thorax, upper back, neck, and lower face—approximately 30% of the total body surface. Initial treatment at another hospital consisted of intravenous infusion of plasma, whole blood, and fluids. Petrolatum (Vaseline) gauze dressings were applied to the burned areas. Initial laboratory studies showed a peripheral white blood cell count of 12,300 per cubic millimeter, with a normal differential count. His urine contained a trace of albumin, with a few casts and rare white blood cells. During the first 24 hours, his urinary output was 60 to 90 cc. per hour, and his temperature rose to 101.6 F (38.7 C). He received 600,000 units of penicillin twice daily in addition to tetanus toxoid, morphine sulfate, and orally given fluids. On Jan. 10, the day after he re-

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ceived the burn, a débridement was done and petrolatum gauze dressings reapplied. The patient was transferred to the West Haven Veterans Administration hospital the next day for more prolonged care.

His medical history and a systemic review were not significant. Examination on Jan. 11, 1955, revealed that dressings covered the described burned parts of a well-developed, well-nourished alert young adult male. His temperature was 101.6 F, his pulse rate was 104 per minute, and his blood pressure was 124/78 mm. Hg. There were 20 respirations per minute. His hair was singed. First and second degree burns were noted on the neck, lips, and alae nasi. The throat was slightly edematous. No other abnormal physical findings were present. Laboratory data on admission were as follows: The white blood cell count was 8,800 per cubic millimeter, with 66% neutrophils, 30% lymphocytes, 3% monocytes, and 1% eosinophils. The specific gravity of the urine was 1.013, and there was 2+ albumin. Microscopic examination of the urine showed 10 to 15 white blood cells per high-power field. Treatment consisted of administration of 300,000 units of aqueous procaine penicillin G twice daily and 0.5 gm. of streptomycin once daily. The patient received a regular diet.

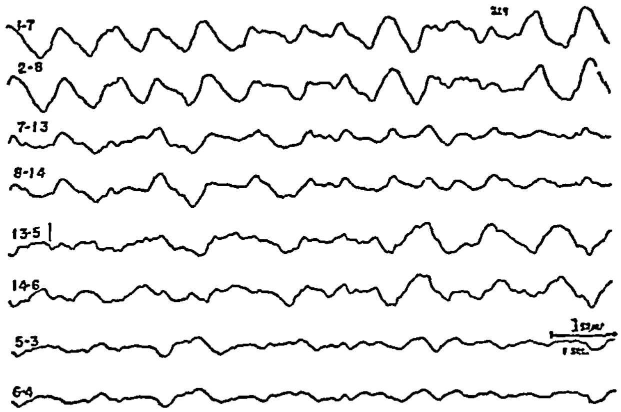

Fig. 1.—Electroencephalogram taken on Jan. 23, one hour after removal of urethan-soaked dressing. Patient was unresponsive. Continuous high-voltage 1 to 2 per second waves seen in all leads. This is consistent with coma. 1-7, left frontal-left anterior temporal; 2-8, right frontal-right anterior temporal; 7-13, left anterior temporal-left posterior temporal; 8-14, right anterior temporal-right posterior temporal; 13-5, left posterior temporal-left occipital; 14-6, right posterior temporal-right occipital; 5-3, left occipital-left parietal; 6-4, right occipital-right parietal.

Hospital Course.—On Jan. 12, 1955, the dressings were changed in the operating room, with the patient under general anesthesia; second degree burns were found on the right upper extremity, with marked edema from the finger tips to the axilla. Second and first degree burns were present on the left forearm and the upper third of the back. There was no edema on the left side. Burned areas were washed with hexachlorophene (pHisoHex) and sterile saline solution, and dry dressings were applied. Although a low-grade fever persisted from the time of admission until Jan. 21, the urine became clear of albumin and white blood cells. The patient was ambulatory on Jan. 13, and he showed no signs of complicating illness. There were no changes in his status until Jan. 18, when dressings were again changed, with the patient under general anesthesia. The dressings were soaked twice daily with a 0.5% solution of acetic acid alternated with 2,000 cc. of a 10% urethan solution with penicillin added. The patient continued his satisfactory course until Jan. 21. He was ambulatory, with good appetite and adequate urine output.

Jan. 21 was the first day of toxic manifestations. Dressings were again changed, with the patient under general anesthesia. During the procedure, the pulse rate increased from 80 to 120 per minute. He remained drowsy for the next 24 hours. The pulse rate varied between 120 and 160 per minute. There was some nausea and vomiting. The administration of antibiotics was continued. Soaking of the dressings with the acetic acid solution was stopped, and the dressings were soaked with the urethan-penicillin solution every three hours. On Jan. 22, lethargy, nausea, and vomiting persisted. The heart rate remained at 160 per minute and the blood pressure was 120/70 mm. Hg. The patient became increasingly sleepy, and his pupils were widely dilated and reacted sluggishly to light. The abdomen was flat and nontender. Peristalsis was audible. On Jan. 23, the patient was areflexic and unresponsive to anything but extreme pain, which made him move but slightly. His condition resembled that of a patient in deep barbiturate narcosis, except that he had a very rapid pulse rate, 160 per minute, and full, deep respirations at a rate of 20 per minute. It was then realized that his symptoms could be the result of a systemic effect of urethan. The urethan-soaked dressings were removed and dry ones applied. He had been bathed with approximately 28,000 cc. of urethan solution containing a total of more than 2,500 gm. of urethan in the interval from Jan. 18 to 23. Laboratory examination revealed that there were 34,400 white blood cells per cubic millimeter, with 96% neutrophils, 3% lymphocytes, and 1% monocytes. The hematocrit value was 46%. There was 27 mEq. of carbon dioxide and 101 mEq. of chloride per liter of serum. The blood urea nitrogen level was 18 mg. and the nonprotein nitrogen level 38.5 mg. per 100 cc. The patient's spinal fluid was normal. An electroencephalogram taken within one hour of the removal of the urethan-soaked dressing showed continuous high-voltage 1 to 2 per second waves in all leads (fig. 1). This was consistent with coma.

On Jan. 24, the patient could be aroused by the calling of his name. He responded accurately to simple questions and was oriented. There was marked nystagmus on lateral gaze to either side. His pupils were widely dilated and did not react to light. Tendon reflexes could not be elicited. In the afternoon, he wakened fully. Later in the day his temperature rose to 104 F (40 C). His white blood cell count was 24,000 per cubic millimeter, with 94% neutrophils, 4% lymphocytes, and 1% monocytes. The hematocrit value was 48%, and the prothrombin time was 25% of normal (Quick method). The blood urea nitrogen level was 63 mg. and the nonprotein nitrogen level 88 mg. per 100 cc. There was 27 mEq. of carbon dioxide and 100 mEq. of chloride per liter of serum. There was 47% excretion of intramuscularly injected phenolsulfonphthalein in two hours. The patient's icteric index was 5.6 units. An electroencephalogram, taken 24 hours after the previous one, with the patient awake, showed that the slow activity was still present (fig. 2).

On Jan. 25, the patient's orientation was less accurate than on the preceding day. He could not cooperate fully during examination. The nystagmus persisted, the conjugate gaze to the right and to the left was incomplete, and the pupils remained widely dilated and fixed. The deep tendon reflexes were barely active. Bilateral Babinski signs were observed. The white blood cell count was 6,000 per cubic millimeter, with 92% neutrophils, 5% lymphocytes, and 3% monocytes. The hematocrit value was 36%, and the prothrombin time was 22% of normal. The blood nonprotein nitrogen level was 81 mg. per 100 cc. There was 30 mEq. of carbon dioxide and 108 mEq. of chloride per liter

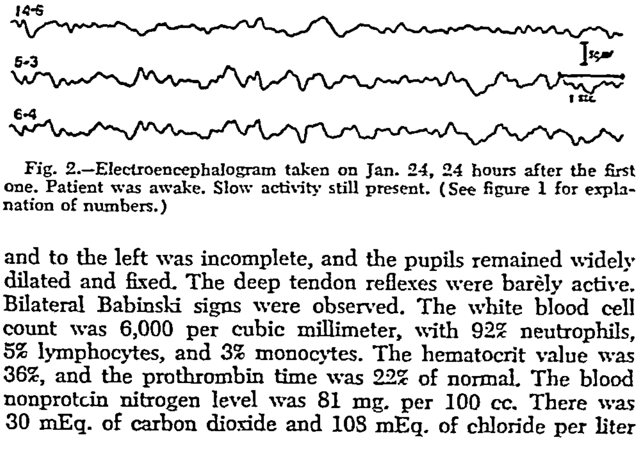

Fig. 2.—Electroencephalogram taken on Jan. 24, 24 hours after the first one. Patient was awake. Slow activity still present. (See figure 1 for explanation of numbers.)

of serum. An electroencephalogram was taken, 24 hours after the previous one, when the mental status of the patient had begun to deteriorate; slow activity was still evident (fig. 3).

On Jan. 26, the patient was disoriented, preoccupied with his discomfort, and difficult to communicate with. Nystagmus was still present, but extraocular movements were full in all directions. The pupils were less dilated. During the afternoon, he became delirious and began to hemorrhage from nose and rectum. Wide areas of ecchymosis developed. An electroencephalogram was taken, 24 hours after the third one, with the patient disorientated; the slow activity had not resolved (fig. 4). On Jan. 27, the patient gradually lapsed into coma. His blood pressure was not obtainable. Hemorrhage was profuse from all body orifices. Vigorous efforts were made to balance blood loss by transfusion, and a total of 2,800 cc. of whole blood was given. Bleeding continued, however, and the patient died at 6 a. m. on Jan. 28, 1955.

Comment

The clinical findings in this case consistent with the previously described systemic effects of urethan were (1) profound anesthesia without depressed respiration, (2) nausea and vomiting, (3) initial increase in the number of white blood cells, with most of them polymorphonuclear, (4) subsequent leukopenia, (5) hemorrhage, (6) renal damage, and (7) hepatic injury. The neurological signs, in addition to anesthesia, attributed to the effects of urethan included nystagmus, disorder of conjugate eye movements, and the Babinski sign. The dilated pupils may have been the result of administration of methantheline (Banthine) bromide for control of nausea and vomiting. The terminal delirium and coma would be expected with hepatic and renal failure.

To our knowledge, the effect of urethan poisoning on the electroencephalogram in man has not been described previously. Observations of electroencephalographic changes during urethan narcosis in rabbits[7] indicated findings similar to those seen in this case: high-voltage ⅓ to 3 per second waves. In a study of anesthetic drugs, French and co-workers[8] noted similar electroencephalographic changes during barbiturate anesthesia, and they postulate the effect of these agents to be on the reticular substance of the brain stem. It is conceivable that urethan has similar action. The presence of nystagmus and the disorder of conjugate eye movement also suggest damage to brain-stem centers. The persistence of slow activity in the electroencephalogram after anesthesia had subsided is interpreted as evidence of diffuse brain damage. This is in keeping with other observations of electroencephalographic changes after brain injury. Nausea and vomiting have been noted when urethan is administered orally, and the symptom is generally thought to be due to local irritation of the gastric mucosa. It seems more likely that this effect is not a local irritation of the stomach but is mediated through central nervous system mechanisms, most likely in the brain stem.

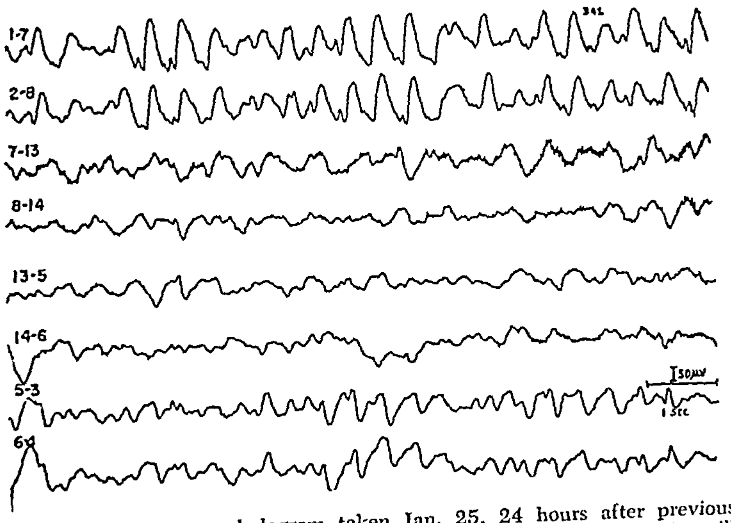

Fig. 3.—Electroencephalogram taken Jan. 25, 24 hours after previous record. Mental status of patient had begun to deteriorate. Slow activity still evident. (See figure 1 for explanation of numbers.)

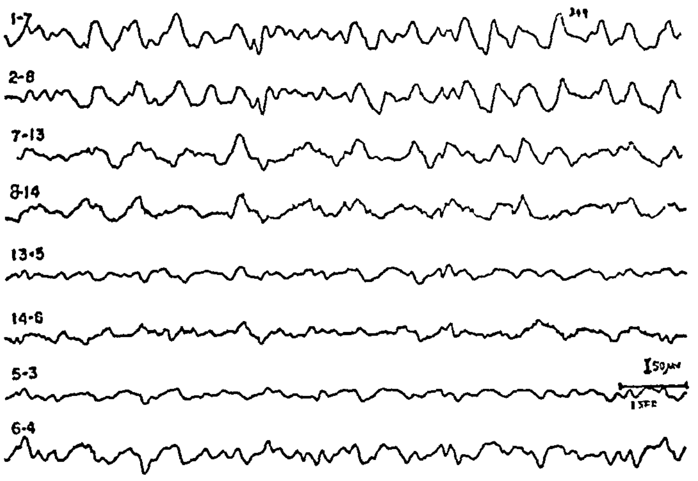

Fig. 4.—Electroencephalogram taken Jan. 26, 24 hours after third examination. Patient was disoriented. Slow activity not resolved. (See figure 1 for explanation of numbers.)

Once absorbed, urethan is rapidly broken down into carbon dioxide, ethanol, and ammonia. Ninety per cent is eliminated through the lungs in 24 hours, and an additional 9% is excreted through the kidneys in a similar period. The remaining 1% is widely distributed in body tissues.[9] The rise in the nonprotein nitrogen level is evidence of renal damage. The elevation of the icteric index and the prolonged prothrombin time signified hepatic injury and bone-marrow depression and were quite evident in this case. With new antibiotics available, topical use of urethan for control of infection should be discouraged.

111 Sherman Ave., New Haven (Dr. Levy).

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MENINGOENCEPHALITIS IN INFECTIOUS MONONUCLEOSIS

REPORT OF A CASE TREATED WITH CORTISONE

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Capt. Perry Berg
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In recent years an ever-increasing number of case reports [1] have directed clinical attention to neurological involvement in infectious mononucleosis. This involvement has been shown to be as diffuse and variable as the classically protean character of the systemic manifestations of the disease. The use of steroids in the treatment of infectious mononucleosis has gained general acceptance since the first description by Doran and Weisberger.[2] Fiese and co-workers [1f] have reported a case of virus encephalomyelitis (Guillain-Barré syndrome) complicating infectious mononucleosis in which there was recovery coincident with the administration of cortisone. A review of the literature fails to reveal any other cases with significant neurological involvement treated in this fashion. The present report deals with a case of diffuse meningoencephalitis in which the patient responded dramatically after the institution of steriod therapy.

A 19-year-old hospital corpsman was well until Aug. 23, 1955, at which time he noted the onset of malaise, lethargy, and insomnia. He was seen in the dispensary, where no abnormal physical findings were noted, and the patient was permitted to rest in quarters. His symptoms abated somewhat with bed rest. However, on Sept. 3, 1955, the patient awoke with a marked exacerbation of his weakness, fatigue, and malaise and developed chills and a fever, with a temperature of 103 F (39.4 C). He had dysphagia and marked anorexia. The patient was hospitalized with a diagnosis of fever of unknown etiology. Upon initial physical examination, the patient had large tender cervical, anterior and posterior, adenopathy; enlarged tonsils covered with a thin purulent exudate; multiple petechial hemorrhages of the soft palate; bilateral axillary and right epitrochlear adenopathy; hepatomegaly; and splenomegaly. Slight stiffness of the neck on passive flexion was noted, but is was felt that this was related to the tender cervical adenopathy. On the basis of the clinical picture, a presumptive diagnosis of infectious mononucleosis was made, and the patient was started on therapy consisting primarily of a diet for hepatitis, vitamin supplements, bed rest, and general supportive care.

On the initial laboratory studies the white blood cell count was 10,200 per cubic millimeter, with 30% polymorphonuclear cells and 70% lymphocytes, of which 10 were of the atypical variety. Liver studies revealed a serum bilirubin level of 0.78 mg. per 100 cc. (with 0.4 mg. per 100 cc. direct and 0.38 mg. indirect), a cephalin flocculation of 2+ at 24 hours and 3+ at 48 hours, and a thymol turbidity of 16.7 units. The initial heterophil titer was 1:56, with a titer of 1:14 on guinea pig absorption and no titer with beef erythrocyte absorption. The remainder of the laboratory studies were entirely within normal limits.

The patient continued to have a persistent fever, with temperatures of 99.8 to 101.8 F (37.7 to 38.8 C) daily, and had progressive systemic symptoms. On the seventh hospital day cortisone therapy was instituted. His temperature rapidly fell to normal, and his systemic symptoms quickly disappeared. The patient did very well and was convalescing without incident except for an episode of epistaxis on the 17th hospital day. Dosage of cortisone was slowly tapered, and therapy discontinued after seven days. On the 19th hospital day the patient again became febrile and malaise and generalized weakness markedly increased. Physical examination at that time was entirely negative. On the following day his temperature rose to 103 F (39.4 C), and he subsequently developed nuchal rigidity. Lumbar puncture at that time revealed an opening pressure of 360 mm. H_2O, clear fluid, and a cell count of 21, all polymorphonuclear cells. The protein level was 61.5 mg. per 100 cc., and the sugar and chloride levels, serology, and colloidal gold curve were all normal. Physical examination revealed an alert well-oriented male. The entire neurological examination was within normal limits. Blood cultures were drawn, and after 12 hours a gram-positive coccus appeared to be growing on one of these. The cerebrospinal fluid was negative on smear and cultures. Although an infectious mononucleosis type of meningoencephalitis was suspected, the one early presumptive positive blood culture led us to treat the patient with large doses of sulfadiazine and penicillin. At this time, the patient had a second episode of epistaxis, which was controlled by packing and vasoconstrictors locally applied. Antimicrobial therapy was continued for seven days without any real abatement in fever, symptoms, or clinical signs. During this period neurological deterioration of the patient was noted. He first became unable to recognize his visitors and then developed generalized muscular twitchings, fine tremor of the tongue, and an intention tremor of the hands. Shortly thereafter a horizontal nystagmus was noted, and his speech became progressively slurred. He became more confused and was disoriented as to time and space. The patient developed progressive generalized muscle weakness and was unable to maintain a sitting posture. The Romberg sign was present, adiadochokinesia was noted, and muscle incoordination and weakness made self-feeding almost impossible. The reflexes were equal; no pathological reflexes were noted. The final laboratory studies revealed that the previously reported coccus in the one blood culture was Micrococcus (Staphylococcus) pyogenes var. albus, and it was considered to be a laboratory contaminant. All other blood cultures (five in number) and the culture of the cerebrospinal fluid were negative.

Therefore, on the 26th hospital day, therapy with both penicillin and sulfadiazine was discontinued, and the patient was started on therapy with cortisone, 300 mg. per day, in keeping with the diagnosis of infectious mononucleosis with associated meningoencephalitis. A repeat lumbar puncture done on this day revealed an initial pressure of 160 mm. H_2O; 47 cells, all lymphocytes; and total protein level of 131 mg. per 100 cc. The sugar and chloride levels, serology, and smear were normal. An interim agglutination test for heterophil antibodies revealed a titer of 1:224, with no absorption by guinea pig kidney and complete absorption by beef erythrocytes. The patient responded very dramatically to cortisone therapy, with lysis of his fever in 36 hours. Within this same period notable clearing of the sensorium occurred, as well as resolution of the nystagmus and tremor of the tongue. By 48 hours the diffuse muscle twitchings were no longer noted and all cerebellar signs were absent. Within 72 hours almost all neurological signs completely cleared. The patient convalesced without further event. A slight residual intention tremor of the hands persisted, as did a slight amount of emotional lability. Both of these symptoms were well controlled with administration of phenobarbital, ½ grain (30 mg.) three times a day. The patient is now completely asymptomatic and has returned to duty.

Comment

In infectious mononucleosis, a perivascular infiltration composed of both normal and abnormal lymphocytes is found in various organs of the body. It is believed that these cells are not invasive, but rather a result of metaplastic changes of reticuloendothelial cells already present in the involved tissues.[3] The perivascular infiltration is not distributed uniformly in the body, and, in a given patient, it may be most pronounced in the liver, kidney, heart, lungs, or the central

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important factor in this patient's inability to mobilize antibodies to vaccinia was the suppressive effect of cortisone therapy, since her leukemia was under good control and administration of gamma globulin failed to alter the course of the vaccinia infection. The patient also had a herpes simplex infection that conceivably might have disseminated under the cortisone influence, but cultures from the various lesions revealed vaccinia virus. It would seem unwise to introduce live virus into patients with leukemia when they are receiving cortisone therapy, as danger of dissemination of the virus exists.

Summary and Conclusions

A fatal case of generalized vaccinia occurred after vaccination in a patient who was on cortisone therapy for chronic lymphocytic leukemia. The introduction of live viruses into patients receiving cortisone may be unwise, and additional studies in this respect seem indicated.

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MEDICINE AT WORK

THE AUTOMOBILE—A CHALLENGE TO MEDICINE

DOCTORS HAVE INTIMATE KNOWLEDGE OF SMASH-UPS. ARE THEY LOGICAL LEADERS IN AUTO SAFETY?

On at least a dozen fronts this month, a problem with the familiarity of a street scene is being attacked as diligently as any group of physicians ever attacked an epidemic. The problem is motor-traffic casualties, and more and more doctors are finding themselves at the crossroads.

For decades, nonmedical experts have seen the tire-writing on the pavement, until now it reads: A traffic death in the United States on the average of every 14 minutes, an injury every 25 seconds. They point to the fact that automobiles have killed 150,000 more people than have lost their lives in all our nation's wars put together. The death toll rises yearly.

Does that constitute a disease? Something of an answer came last June when the House of Delegates of the American Medical Association—viewing it as a medical problem "of major importance" affecting "more persons than does all illness known today"—voted to create a special Committee on Medical Aspects of Automobile Injuries and Deaths. Within a few weeks that committee, under Dr. Fletcher D. Woodward of Charlottesville, Va., will meet to determine how such factors as driver-license standards, motor-vehicle design and equipment, medication to drivers, and improvement of first-aid procedures at accident scenes might be of legitimate interest to the medical profession.

What Is Happening Now

Meanwhile, attack on the nationwide problem includes these other current developments:

—A documentary film, "On Impact," produced jointly by the A.M.A. and the Ford Motor Company, began appearing on television screens across the nation two weeks ago to dramatize prevention of automobile accidents.

—On Oct. 8, the World Medical Association began detailed study of an urgent report from an Australian delegation calling for "consideration of the subject of road accidents."

—Earlier this month, the A.M.A. Women's Auxiliary accented safety-consciousness at a workshop in Chicago, urging that Congress appoint a national body to regulate safety standards in auto construction.

—In the past week, also in Chicago, the National Safety Congress met to consider new ways to fight slaughter on the highways.

—A U. S. House subcommittee is preparing for public hearings in a few months to consider the role medicine might play against the increasing number of traffic deaths.

—Engineers at the Cornell Aeronautical Laboratory are now completing the prototype of an experimental automobile designed to let occupants walk away from a 50-mile-an-hour head-on collision.

—The World Health Organization is putting out a list of some two-dozen suggested conditions that should bar issuance of vehicle licenses to unqualified drivers.

—An intensive investigation of personal and interpersonal factors in motor-vehicle accidents is under way at the University of Colorado and the Fitzsimons Army Hospital. Similar studies still are going on at the Harvard School of Public Health.

—Continuing interest in traffic safety as a medical problem is reflected in the fact that this is the 16th article on auto accidents to appear in The Journal in the past year.

—The U. S. Public Health Service is now expanding its home-safety unit into a new "accident prevention program" covering highway deaths and injuries as well.

—This week, the International Association of Chiefs of Police invited physicians, as either individuals or medical societies, to work with the association in helping to solve the traffic-casualty problem.

—New York State is putting final touches on Governor Harriman's plan for a scientific study of the human factors in traffic accidents.

Chairman Woodward of the new A.M.A. committee points out that, significantly perhaps, there is no coordinated direction in the many-angled fight for highway safety. He says: "Dozens of agencies are investigating, are viewing with alarm, are making surveys and announcing findings, and are trying to correlate.

But so often the result is overlap, duplication and repetition of old facts and theories. There is strong need for leadership." He suggests that physicians may be the logical leaders in any movement toward reduction of traffic casualties because of their biological science background and their intimate knowledge of crash effects and the problems of human behavior that might figure in the smashups.

The medical profession thus is in a position not only to gauge aspects of auto design and to set up physical standards in the reissuance of revoked driver permits but also to guide research and to advise on the many physical conditions that determine whether a patient should drive.

Real Cow and Fake Calf

You might chuckle at the curious plight of Mr. and Mrs. Milo Ewing of Denver several years ago when a 1,300-lb. cow, fleeing from a stockyards, leaped off an overpass and landed kerplunk on the roof of the couple's car as they were driving along. But it is no laughing matter to consider the hallucination of a weary truck driver who told Harvard researchers how he was injured when he "saw" a calf in the roadway. He swerved, overturning the truck. It turned out there was no calf—just a "dream image" common to many people who drive when they are too tired.

Why does a man drive when he is too tired—and what is "too tired?" Why does the motorist speed beyond the capacity of his reflexes—and what is that capacity? Why does he persist in driving while drunk? Why does he react as he does in traffic and to traffic enforcement?

These questions indicate a psychological base to the traffic-safety problem. A survey in 11 northeastern states revealed that drivers are getting progressively more irritable in the squeeze of mounting traffic congestion. Research at Harvard shows that a motorist's attitudes and personal adjustments are more important in driving safety than his physical skill, vision, or reaction time. At the same time, Dr. Leonard Scheele, the former U. S. surgeon general, calls for periodic reassessment of driver health and skills at license renewal time. In one state, South Dakota, presumably you can get a driver's license if you are totally blind; there are no visual requirements.

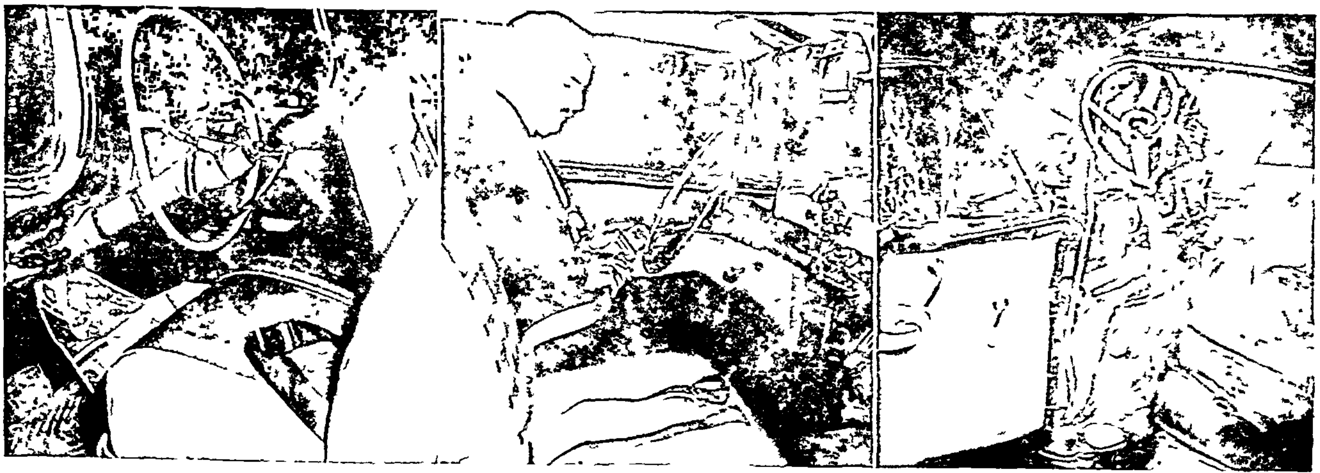
Dr. DuPont Guerry III, chairman of the department of ophthalmology at the Medical College of Virginia, is recommending that a board of ophthalmologists, working through the A.M.A., urge states to determine "vital functions" relating to auto safety. He says that one of the most pressing problems is the wrap-around windshield, with its "terrific visual distortion due to prismatic effect, increased glare because of the focusing of extraneous light . . . and insuperable diplopia from ghost images."

The curved windshield is just one aspect of auto design accused of hampering auto safety. Dr. Horace E. Campbell of Denver points out: "There has been no real change in construction of the motorcar bumper since it was first installed as an accessory some 35 years ago. Many of our present serious crashes would be minor incidents if the bumper had been improved as much as the motor." Only recently have some auto makers begun to adopt safety as a selling point: pop-out windshields, hold-tight door latches, padded instrument panels, collapsible steering wheels, more firmly anchored seats, and shoulder straps.

But no single safety device has been more effective in a crashing auto than the properly installed seat belt. On this the experts agree, especially in a market of high speed, power brakes, and trigger-happy driver feet.

Doctor and Wife Saved

Not long ago Dr. and Mrs. George Spielman of Mandan, N. D., were persuaded by another Mandan physician to install safety belts in their car. As the couple started out on a vacation trip, another auto turned into their path. Dr. Spielman slammed on the brakes, and swerved to avoid a crash. His auto somersaulted into a ditch and landed on its top as the windshield shattered. Inside, he and his wife were suspended safely by their seat belts. In another case, two cars crashed head on. The couple in one car with seat



Air Force Lieut. Billy J. Yeiser installed a seat belt in his car last spring. Within 24 hours his auto was struck head on, *left*, by a car in southern Illinois. He suffered only minor injuries, while two persons were killed and six hurt in the other auto. *Center*, proper use of seat belts. *Right*, the human-impact result of another head-on collision in which there were no seat belts (National Safety Council photos).

belts were released from a hospital the next morning after observation. There were no seat belts in the other auto; one occupant was killed, and the other was in the hospital for two months.

State and county medical societies are just beginning to get into the traffic-safety picture with committees of their own, as the result of last June's A.M.A. resolution, but a few of them have been active in the field for years. In Virginia, for example, several county medical societies made a joint appeal to the governor and the legislature for tests of suspected drunken drivers and for mandatory jail sentences of at least 24 hours against those convicted.

Is It a New Medical Specialty?

The more some physicians look into traffic safety, the more they seem to see the possibility of a new medical specialty (one general practitioner suggested it be called "medicotrafficology"). In the traffic-safety field they find essentials of over a half-dozen other specialties: preventive medicine, psychiatry, epidemiology (the Harvard school suggests that state motor-vehicle bureaus hire full-time epidemiologists), neurosurgery, ophthalmology (the Harvard school claims that carbon monoxide inhaled from smoking three cigarettes has the same anoxic influence on night vision as going to an altitude of 7,500 ft.), toxicology, orthopedics, and industrial health. (The accident rate of the Third Avenue transit system in New York City was cut in half by a company medical program that included psychological tests for vehicle operators. Absenteeism went down, there was a reduction of 3,000 accidents a year, and the company saved $100,000 in compensation and sickness benefits.)

But it is in the economics of the problem that physicians can see tremendous waste in dollars that might be used to save human life. In the past 40 years in the United States we have spent 75 billion dollars for roads and nearly two and a half trillion dollars for new vehicles, accessories, and fuel. Traffic accidents last year cost 4.4 billion dollars, according to the U. S. Public Health Service.

Yet, the Association of Casualty and Insurance Companies estimates that less than 4 million dollars a year is spent for all forms of highway safety and that "a miniscule of that amount went into the search for an answer to the riddle of the human being at the wheel." So, to many, the traffic problem has become a major medical problem by the very nature of its bloody eruption into a socioeconomic crisis. As Dr. Woodward puts it: "When one car in twelve is involved in a serious crash each year, when speed is a factor in one-third of our fatal accidents, when the drinking driver is in one-fourth of our fatal accidents, when the automobile death rate as figured in man years of life lost ranks next to our main killers of cardiovascular disease and cancer, it is time indeed to answer Cain's query and say: 'Yes, I am my brother's keeper.' "

COUNCIL ON PHARMACY AND CHEMISTRY

Report to the Council

The Council has authorized publication of the following report.

H. D. Kautz, M.D., *Secretary.*

It is generally recognized that the final evaluation of the toxicity of a chemical encountered by humans should be in terms of its effect on man. The following report concerns the first experimental study of the storage, excretion, and possible clinical effects in man of chlorophenothane (DDT) given in many small daily doses. By relating excretion to dosage, the study makes practical the quantitative estimation of the dosage for persons with extensive occupational exposure to DDT, and thus eventually makes possible evaluation of the effect of DDT on man after years of exposure. This is important, for DDT continues as the predominant residual insecticide for agricultural and public health use. Any effects of repeated exposure would appear on the average most promptly, most frequently, most diversely, and most severely among persons whose exposure has been long and intensive.

Bernard E. Conley, *Secretary*
Committee on Pesticides.

THE EFFECT OF KNOWN REPEATED ORAL DOSES OF CHLOROPHENOTHANE (DDT) IN MAN

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Much knowledge is available regarding the effect of repeated doses of chlorophenothane (DDT) on a variety of animals. Significant interspecies variation has been found in its toxicity when given orally, the storage of DDT in fat, and the conversion of DDT to 1,1-dichloro-2,2-bis(*p*-chlorophenyl)ethylene (DDE). Some other aspects of the pharmacology of DDT have not been investigated sufficiently to determine whether interspecies differences are present. A final evaluation of the effect of DDT on man must be made with human subjects. The practical importance of the problem is evident from the fact that a greater tonnage of DDT than of any other insecticide is used in agriculture, that DDT occurs regularly in prepared meals,[1] and that it is stored in the fat of most persons in the general population.[2]

From the Communicable Disease Center, Public Health Service, U. S. Department of Health, Education, and Welfare.

Read before the American Association for the Advancement of Science, Panel Discussion on Hazardous Household Chemicals and Agricultural Poisons, sponsored by the Committee on Toxicology and the Committee on Pesticides, American Medical Association, Atlanta, Ga., Dec. 29, 1955.

An investigation was designed with the following objectives: 1. Study of possible clinical effects of different dosage levels. Only those dosage rates were chosen that were estimated to be harmless, for it was not the purpose of the study to cause illness. The highest dosage rate chosen (0.5 mg. per kilogram of body weight per day) is about 200 times greater than the dosage to which the general population is exposed (0.0026 mg. per kilogram per day) but 5 times less than the smallest dosage that is estimated to cause transient, mild sickness (2.5 mg. per kilogram per day). This latter estimate was made on the basis of animal experiments and on the basis of the smallest single dose of DDT known to produce mild illness in man.[3] This estimate should not be confused with the dosage of 2.5 mg. per day (about 0.035 mg. per kilogram per day), which Fitzhugh estimated could be ingested for long periods without injury.[4] 2. Determination of the relationship between oral dosage of DDT and the storage of DDT-related compounds in adipose tissue at equilibrium. Improvement made in chemical methods during the study permitted a third objective to be added: 3. Determination of the relationship between oral dosage of DDT and the urinary excretion of bis(p-chlorophenyl) acetic acid (DDA).

Permission was obtained from the Bureau of Prisons, U. S. Department of Justice, to carry out the experiment using volunteers in a federal correctional institution. The study was explained to almost the whole population of the institution. Detailed explanations were made to those who were interested in participating. The men who tentatively volunteered were examined and were accepted if they proved to be qualified physically and in other ways. The fact that participation was at all times strictly voluntary must be emphasized; each man was free to leave the study at any time.

Methods

The selected volunteers were divided into six groups, three entering the study in February, 1954, and three in May, 1954. As shown in table 1, groups 1 to 3 received dosages of 0, 3.5, and 35 mg. of DDT per man per day, respectively, for periods ranging up to 18 months. Each dose was carried in a capsule of oil containing the appropriate concentration of recrystallized p,p'-isomer of DDT.

Although groups 4, 5, and 6 received the same dosages as groups 1, 2, and 3, respectively, two major changes were made: technical DDT was used, and it was administered as an emulsion in milk rather than in capsules. The capsules were originally chosen for groups 1 to 3 because of their convenience. They were abandoned for groups 4 to 6 in favor of a formulation more nearly like a "natural" residue and also for administrative reasons. The emulsion concentrates were prepared by homogenizing 5 gm. of gum arabic, 90 cc. of water, 10 cc. of 95% ethyl alcohol, and 15 cc. of peanut oil. For groups 5 and 6, the peanut oil moiety of the formulation contained 0.538 and 5.38% of technical DDT respectively. These concentrations were chosen in order that 5 cc. of the two emulsion concentrates would contain 3.5 and 35 mg. of DDT respectively. Before being offered to the men, 5 cc. of the appropriate emulsion concentrate was diluted with milk to a total volume of about 2 oz. Chemical analyses of capsules and emulsions gave values for the concentration of DDT that were in excellent agreement with intended values. Analyses indicated that the emulsions were stable in DDT content for at least two months, a longer period than that required for the experiment, because new supplies of emulsion were prepared at monthly intervals.

Proper dosage for the different groups of men was assured by packaging each capsule and marking each bottle of emulsion for individual volunteers. The capsules, regardless of their DDT content, were identical in appearance. The same was true of the emulsions. The men were told the dosage rates and the design of the experiment before they volunteered, but no volunteer was told his individual dosage. Furthermore, this detail was not revealed to the medical officer stationed at the institution nor to the medical technical assistants. All of the volunteers, irrespective of group, were given capsules (or emulsion) containing no DDT for 17 days at the beginning of the study; the regular doses were begun without notice.

Samples of the meals served the men in the dining hall were analyzed for DDT content to determine the exposure that might be expected from this source. Complete meals for a total of four days were analyzed. The results are shown in table 2. Considerable variation was found among foods and even among whole meals with respect to DDT content; however, the mean

TABLE 1.—*Outline of Experiment*

		Dosage			No of Men					
Type of DDT	Group No	Added, Mg./Man/Day	Total (Range),* Mg /Kg /Day	Case No	Entering Experiment	Completing 17 Predosage Days	Completing 1 Mo of Dosage	Completing 12 Mo of Dosage	Completing 18 Mo of Dosage	Completing Final Examinations
Recrystallized	1	0	0.0021-0.0031	0-8	9	8	7	1	0	5
	2	3.5	0.048-0.059	9-16	8	8	7	1	0	4
	3	35	0.41-0.61	17-25	9	9	8	1	1	7
Technical	4	0	0.0023-0.0034	26-33	8	6	6	3	1	4
	5	3.5	0.038-0.063	34-41	8	8	8	2	0	8
	6	35	0.36-0.57	42-50	9	8	8	6	3	7
Total					51	47	44	14	5	35

* The total dosage included dietary DDT as well as the administered dose. Dietary DDT, resulting from agricultural residues, was estimated at 0.184 mg./man/day on the basis of the analyses of whole meals. The total dosage varied somewhat according to the weight of the men.

daily DDT intake of 0.202 mg. was in reasonable agreement with the value of 0.184 mg. reported by Walker and co-workers[1] for a larger series of sample meals. The value of 0.184 mg. per man per day was used in computing the total daily DDT dosage for each man as shown in table 1, because this value is based on a large number of samples and is the best estimate of the true average now available. This is especially true because the figures in table 2 would agree better with those given by Walker and his colleagues if it were not for the values obtained for breakfast and especially lunch on Aug. 25. The value for the breakfast was associated with the finding of 69.6 ppm of DDT in stewed dried fruit. Except for bread, which showed a concentration of 100.9 ppm of DDT, the DDT content of the lunch was not unusual. There was no record of the kind of shortening used in this bread; however, it was later learned that bread, all of which was baked at the institution, was occasionally made with lard (which contained, on analysis, a relatively high concentration of DDT) rather than with vegetable shortening (which proved to be of low DDT content). In both the fruit and the bread the DDE concentration was relatively low.

Table 2.—*DDT and DDE Found in Typical Meals Served to Volunteers*

Meal	Date, 1954	Total Found, Mcg. DDT	Total Found, Mcg. DDE
Morning			
1	Aug. 25	115.6	16.9
2	Oct. 4	45.1	18.9
3	Nov. 9	54.9	6.8
4	Dec. 9	79.0	33.9
Mean		73.7	19.1
Noon			
1	Aug. 25	204.0	24.8
2	Oct. 4	44.6	23.0
3	Nov. 9	21.6	6.0
4	Dec. 9	26.5	4.1
Mean		74.2	14.5
Evening			
1	Aug. 25	72.5	22.0
2	Oct. 4	51.3	17.2
3	Nov. 9	23.7	16.3
4	Dec. 9	69.1	11.8
Mean		54.2	16.8
Daily Mean		202.1	50.4

Volunteers were checked for previous exposure to insecticides (which in all instances was negligible) and were given a careful symptoms review, a general physical examination, and a variety of laboratory tests prior to their entrance into the project and at six-month intervals thereafter. Particular emphasis was given to the neurological examination and liver function tests, since in experimental animals the major effects of DDT are on the nervous system and the liver. The liver function tests carried out were sulfobromophthalein retention and plasma cholinesterase level. The electrometric method of Michel[5] was used for the cholinesterase determination. Vorhaus and co-workers[6] have shown that plasma cholinesterase level is a significant index of hepatic function. Preliminary studies with monkeys have indicated that some decrease in plasma cholinesterase level might be associated with high DDT dosage levels.

In all instances, fat samples for the determination of DDT-derived compounds were obtained by biopsy, using local procaine anesthesia. Blocking was done around the operative site, and it was generally possible to avoid infiltration of the tissue that was later excised. The biopsy specimen was usually taken through a 1.5-in. incision from the subcutaneous adipose tissue of the abdomen. Body fat content was calculated from specific gravity, which was determined by weighing the individual under water.[7] Analyses for DDT, DDE, and DDA were made by the Schechter-Haller method. The procedure used for adipose tissue has been described by Mattson,[2] and the procedure used for urine has been described by one of us (C. C.).[8]

During the study some of the men left the institution by transfer or parole or on other authority. Whenever sufficient notice was given, the men were completely reexamined shortly before their participation in the project ended. During the course of the study, 126 complete sets of examinations were carried out on the 51 volunteers. Table 1 indicates the number of men in each group who participated for specified periods. Of the 47 men who remained in the study longer than 17 days, biopsy specimens from 35 were taken, and they were completely reexamined after their last dose of DDT. Two men refused the final biopsy but underwent the other tests. Four others were released on such short notice that no final examination was possible, but a biopsy was performed by a private physician after their release. Thus, of the 47 volunteers, only 6 were discharged in such a way that they received no final biopsy or examination.

Results

Condition of Volunteers at Start of Experiment.—The condition of the volunteers on entering the experiment is shown in part in table 3. The men who entered in February varied in age from just under 21 to just over 50 years; those who entered in May varied from just over 21 to a little over 40. All the men except three were essentially normal, not only regarding values shown in table 3 but in other respects as well. Two of the abnormal men (cases 7 and 29) were in control groups and, therefore, not subject to any influence of DDT. They were asymptomatic and afebrile throughout. The patient in case 7 had a white blood cell count that varied from 13,400 to 20,200 per cubic millimeter over a period of several months. He showed as high as 12% of eosinophils, but the differential count was otherwise normal. There was moderate lymphadenopathy. Despite a thorough examination, the underlying cause of the difficulty was not determined. It was established that leukemia was not present. The patient in case 29 had albuminuria and microscopic and other findings consistent with a diagnosis of latent chronic nephritis. Illness did not progress in either subject during the study; in fact, the condition of the patient in case 7 returned toward normal.

The third subject (case 9) had abnormally high sulfobromophthalein retention on initial examination; his plasma cholinesterase value was within normal limits. He received 3.5 mg. of DDT per day and was asymptomatic during the 89 days he remained in the experiment. Because of inadequate notice of his departure from the institution, no final studies were done on this man.

Two volunteers who gave a history consistent with infectious hepatitis were taken into the experiment despite the effect of very large doses of DDT on the liver of experimental animals and, according to one author,[9] of man One man (case 5), a control patient, received no DDT, the other (case 20) received 35 mg. of DDT per day. Jaundice did not recur in these men, and they showed no abnormality in liver function tests during the experiment

Effect on Health—Four men quit the experiment of their own accord One subject (case 0) quit only one day after the first biopsy, thus, except for the biopsy, he was not a part of the experiment. A second man (case 8) from the same control group considered that his health had been injured after a total of 182 days in the study (no DDT given). He refused a final biopsy. Physical and laboratory examination disclosed no abnormality except a dermatitis of the right leg, which he attributed to his participation A volunteer (case 16) who received 3 5 mg of DDT per day also refused a final biopsy and quit just before he was transferred from the institution He had participated for 155 days and had received 138 doses of DDT He had several complaints, including pain every day in every bone, occasional headache, and tearing of the right eye He submitted to complete physical and laboratory examination, and all findings were normal His complaints obviously were of psychoneurotic origin, and even the man himself did not seem to take them seriously One volunteer (case 19) receiving 35 mg of DDT per day quit after 21 days (DDT given last 4 days) He had no specific complaints but was unwilling to continue

Of the total of 37 volunteers who were questioned specifically on the matter just after completion of their participation in the study, only the two mentioned considered that their health had been adversely affected. In one instance of weight loss, the possibility of injury caused by DDT exposure was considered. The subject (case 11) had a history of a 7 kg (15 lb) fluctuation of weight before entering the experiment. His weight loss of 6 kg. (13 lb.) during the study was associated directly with hard physical work in a hot environment. He accepted this explanation and, with the onset of cool weather, regained his weight while continuing to take DDT.

Changes in certain important items that can be measured were tabulated and compared for the six groups for the periods 5 to 6, 7 to 8, 9 to 10, 11 to 12, and 12 or more months of dosage respectively. It was necessary to tabulate changes rather than observed values because, as some men completed their participation, the composition of the sample shifted. For example, the average weight of men in group 1 was less after five to six months than at the beginning of the experiment because a heavy man had dropped out, most of the men who remained had gained weight, and the average change of weight was a slight gain The items examined in this way were weight, hemoglobin level, red blood cell count, white blood cell count, percentage of polymorphonuclear leukocytes, heart rate (at rest, just after exercise, and after two minutes of rest), systolic blood pressure and pulse pressure (at rest and after exercise followed by two minutes of rest), and plasma cholinesterase level. Although changes were observed in all of these values, none were correlated consistently with increased dosage of DDT or with increased duration of exposure Since the changes were random in distribution and not unusual in degree, they must be attributed to normal variation. No significant change in sulfobromophthalein retention was noted. This item was not tabulated because the retention values for most of the men were zero before and after exposure to DDT In a similar way, chest x-ray findings were not tabulated, for they all were essentially normal

TABLE 3—*Condition of Volunteers at Beginning of Experiment*

	Groups Given Recrystallized p,p'DDT					
Group No	1		2		3	
No of Men	8		8		9	
	Range	Mean S E	Range	Mean, S E	Range	Mean, S E
Age, yr	22.5-50.1	30.9±3.4	22.4-48.7	29.5±3.1	20.9-45.8	27.8±2.6
Weight, kg	60-87.7	73.6±3	69.7-77.2	65.6±2	57.7-86.3	74.5±3
Red blood cell count, millions cu mm	4.1-5.5	4.8±0.03	3.9-5.6	4.8±0.05	3.0-6.9	4.9±0.04
Hemoglobin level, gm 100 cc	12.0-14.0	13.3±0.7	13.5-14.5	14.0±0.7	12.0-15.0	13.8±10
White blood cell count, thousands/cu mm	5.4-15.0	9.0±1.0	6.9-9.9	8.6±0.4	5.9-13.8	9.2±1.0
Polymorphonuclear neutrophil leukocytes, %	37-71	55±5	40-71	58±4	42-66	57±2
Heart rate rest, strokes/min	60-85	72±3	64-100	78±5	64-95	88±3
Heart rate, exercise, strokes/min	80-120	99±5	80-135	104±6	92-120	105±4
Heart rate, exercise and rest, strokes min *	−12 to −8	−3.2	−12 to −16	−2.3	−16 to +4	−5.4
Systolic blood pressure, rest, mm Hg	105-152	120±5	100-134	115±4	100-140	121±4
Pulse pressure rest mm Hg	23-55	39±4	35-70	47±2	30-65	46±4
Systolic blood pressure, exercise mm Hg	105-150	121±5	95-130	117±4	105-160	127±7
Pulse pressure exercise mm Hg	25-55	41±4	[illegible]-65	47±5	35-85	58±6
Plasma cholinesterase, ΔpH hr	0.54-1.07	0.84±0.05	0.53-1.10	0.85±0.07	0.60-0.96	0.69±0.04
DDT in fat ppm	3-9	6.9±0.8	4-11	5.1±0.8	4-9	6.6±0.7
DDE in fat ppm	7-26	14.9±2.8	7-16	10.8±1.3	8-19	12.2±1.3

	Groups Receiving Technical DDT					
Group No	4		5		6	
No of Men	8		8		9	
	Range	Mean S E	Range	Mean S E	Range	Mean S E
Age yr	22.9-40.4	28.9±2.0	21.7-33.6	27.5±1.4	22.7-34.8	27.9±1.3
Weight, kg	53.6-81.3	70.4±3	[illegible]-97.2	74.5±5	62.2-97.7	75±2
Red blood cell count millions/cu mm	4.5-7.2	5.3±0.05	4.4-6.3	5.1±0.07	4.8-5.6	5.2±0.06
Hemoglobin level gm /100 cc	13.0-14.5	13.[illegible]±0.6	13.0-15.0	13.4±0.8	13.0-15.5	14.1±0.9
White blood cell count, thousands/cu mm	[illegible]	[illegible]	[illegible]-9.9	7.9±[illegible]	4.4-11.1	8.3±0.8
Polymorphonuclear neutrophil leukocytes %	35-68	52±3	[illegible]	60±3	46-75	50±3
Heart rate rest, strokes/min	56-76	[illegible]±3	60-80	72±2	64-88	76±3
Heart rate exercise, strokes/min	80-136	98±7	80-116	98±4	104-136	116±4
Heart rate, exercise and rest, strokes min *	[illegible]		[illegible] to −8	−1.0	−4 to −24	−4.8
Systolic blood pressure rest mm Hg	98-140	118±5	112-135	122±3	115-130	122±2
Pulse pressure rest, mm Hg	24-50	38±4	35-65	49±3	31-53	46±2
Systolic blood pressure exercise mm Hg	102-140	118±5	118-135	120±2	112-135	123±3
Pulse pressure exercise mm Hg	30-52	41±3	35-65	49±3	[illegible]	48±3
Plasma cholinesterase ΔpH hr	0.72-1.37	0.91±0.09	[illegible]-1.35	0.83±0.09	0.70-1.04	0.86±0.0[illegible]
DDT in fat, ppm	4-13	9.5±1.0	7-11	8.5±0.6	4-12	7.2±1.0
DDE in fat ppm	[illegible]	[illegible]±1.2	[illegible]-13	10.4±0.8	[illegible]-22	8.6±2.0

*Recorded as increase or decrease of strokes per minute compared to the rate for the same person just before exercise followed by 2 min of rest

The initial review of symptoms revealed a great variety of minor complaints. These complaints were not unusual, and the men undoubtedly were predisposed to some of them by their confinement. A small number of minor physical defects was revealed by examination. In subsequent examinations no increase or significant change in abnormal physical findings was discovered. There was some tendency for the volunteers to give fewer compaints at subsequent interviews.

Results of following tests were taken into consideration in the neurological examination: gait, including ability to walk on toes and heels; coordination including Romberg, finger to nose, heel to shin, adiadochokinesia, rebound, past-pointing, tremor, handwriting, and "tongue twisters"; deep reflexes, superficial reflexes, and clonus; muscle strength, including all major movements of the neck, shoulder, elbow, wrist, fingers, hip, knee, and ankle; sensation, including light touch, pinprick, two-point discrimination, position sense, vibration sense, stereognosis, and differentiation of heat and cold; and function of the cranial nerves, including identification of an odor, visual fields, reactivity of pupils, extraocular movements, strength of bite, sensation of the face, coordination and strength of facial muscles, hearing, pharyngeal reflex and voice, and protrusion of the tongue. All of the participants remained normal in regard to these neurological tests; of particular interest, they showed no loss of coordination and no indication of tremor.

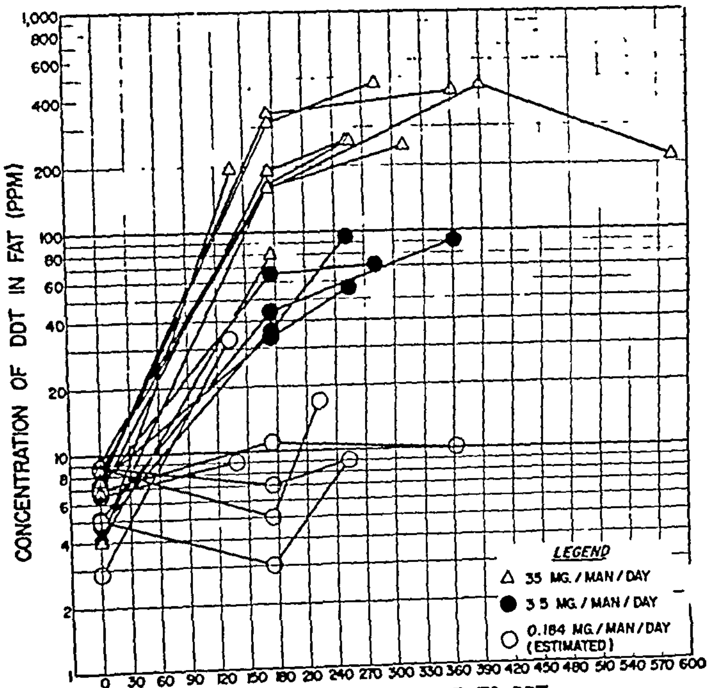

Fig. 1.—Storage of DDT in the subcutaneous fat of volunteers given indicated doses of recrystallized *p,p'*-isomer of DDT.

In contrast to the random and normal variation encountered in other tests, the values for the storage and excretion of DDT-derived materials showed a strong correlation with dosage and with duration of exposure. In conclusion, during the entire study, no volunteer complained of any symptom or showed any sign of illness that did not have an easily recognized cause clearly unrelated to exposure to DDT.

Storage of DDT-Derived Materials.—The storage of DDT in subacutaneous fat by groups 1, 2, and 3 is shown in figure 1 and that by groups 4, 5, and 6 in figure 2. It is clear that storage was directly proportional to dosage. The graphs suggest that, at the dosages used, human males achieve storage equilibrium for DDT in about a year, but further observation is necessary to establish this conclusion firmly. The absolute variation was greater among the higher storage level values, but, as shown by a comparison of the coefficients of variation in table 4, the relative variation remained about the same.

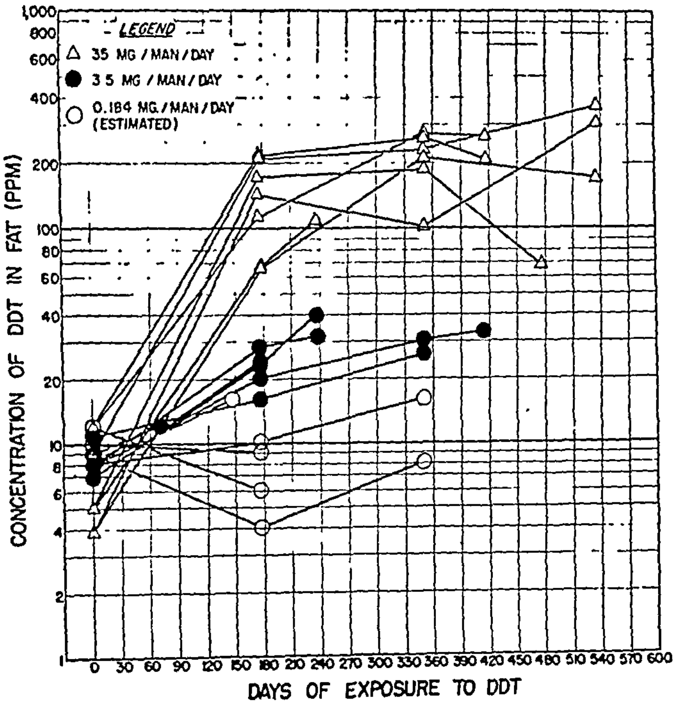

Fig. 2.—Storage of DDT in the subcutaneous fat of volunteers given indicated doses of technical DDT.

An unexpected finding was the difference in the amount of storage at the same dosage in connection with recrystallized DDT and technical DDT respectively. Rats show a difference in this regard, but it is smaller in degree and opposite in direction; that is, under conditions of equal exposure, rats store more technical DDT than recrystallized DDT. At a dosage of about 0.5 mg. per kilogram of body weight per day for 10 months or more, the volunteers stored recrystallized DDT in their fat at a concentration of 216 to 466 ppm (mean, 340 ppm). At the same dosage for the same period, other volunteers stored technical DDT at a concentration of 101 to 367 ppm (mean, 234 ppm). Unfortunately, it is impossible to determine whether the difference was associated with the character of the DDT samples or with the formulations in which they were administered. As shown in table 5, however, the level of statistical significance for the difference between the storage of recrystallized and of technical DDT is very nearly as great as the signi-

TABLE 4.—*Variability of Storage of DDT at Different Storage Levels*

		Duration of Exposure, Mo.					
		0		6		12	
Group*	No. of Men	Mean Storage, Ppm	$V\bar{x}$,† %	Mean Storage, Ppm	$V\bar{x}$,† %	Mean Storage, Ppm	$V\bar{x}$,† %
3	8	6.5	10.0	202	15.3	...	...
6	6	7.7	20.2	155	15.6	210	12.0

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* For each group, the same persons were considered in each calculation.

† Coefficient of variation of the standard error of the mean.

ficance of differences based on dosage and on duration of exposure calculated in the same way. These latter differences, of course, have a simple, biological explanation. The statistical analysis indicates that the difference between the storage of recrystallized and of technical DDT cannot be ignored but should be the subject of further studies in the hope that a reasonable biological and/or chemical explanation may be found.

Table 5.—*Statistical Significance of Differences in DDT Storage in Human Fat Associated with Dosage, Duration of Exposure, and Type of DDT*

Condition	Comparison	Statistical Level of Difference, %	
		Duration of Exposure, Mo.	
Type of DDT	Dosage, Mg./Man/Day	3-6	7-18
Technical	0 vs. 3.5	<95	>99
	3.5 vs. 35	>99	>99
Recrystallized	0 vs. 3.5	>99	>99
	3.5 vs. 35	>99	>99
		Dosage, Mg./Man/Day	
Type of DDT	Duration of Exposure, Mo	3.5	35
Technical	0 vs. 3 6	99	>99
	3-6 vs. 7-18	>99	>95
Recrystallized	0 vs. 3-6	>99	99
	3-6 vs. 7-18	>99	>95
		Dosage, Mg./Man/Day	
Duration of Exposure, Mo.	Type of DDT	3.5	35
3-6	Tech. vs. Recryst.	>99	<90
7-18	Tech. vs. Recryst.	>99	>95

Storage of DDE in subacutaneous fat is shown in table 3 and figure 3. In the presence of ordinary dietary exposure to DDT, the storage of DDE showed about the same variability as the storage of DDT. For the men entering the experiment the average storage of DDE was 11.2 ±0.74 ppm, giving a coefficient of variation for the standard error of 6.0%; the average storage of DDT was 7.4 ±0.37, giving a coefficient of variation of 5.0%. Men who ate recrystallized DDT showed a definite increase in the absolute amount of DDE stored. After six months at a dosage of 35 mg. per man per day, eight men showed an average DDE storage of 32.6 ±7.0 ppm as compared to 12.3 ±1.5 ppm for the same individuals upon entering the experiment. There was a further increase of DDE storage during additional months of exposure; however, DDT was stored in so much greater concentrations that the relative storage of DDE decreased sharply. Thus, after six months at a dosage of 35 mg. per man per day, eight men stored only 14% of their total DDT-derived material in the form of DDE, as compared to 65% for the same persons at the beginning of the experiment.

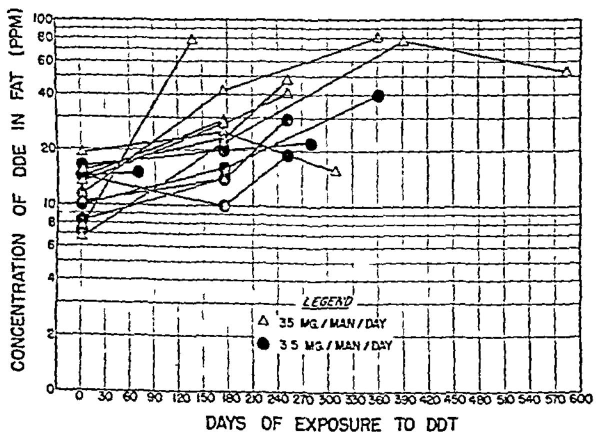

Fig. 3.—Storage of DDE in the subcutaneous fat of volunteers given indicated doses of recrystallized *p,p'*-isomer of DDT. For graphic clarity, values for the control group have not been plotted.

The storage of DDE by men who ate technical DDT presented a different picture. Until 18 months of exposure, there was no clear evidence that those men stored any more DDE after exposure than they did before; however, at 18 months, the only three samples available showed DDE concentrations of 85, 42, and 28 ppm. Although these values constituted only 16% of the total storage of DDT-derived material, they are all well above average for general population figures and thus indicate the conversion of technical DDT to DDE in the volunteers. The question is complicated by the fact that the chemical method does not permit measurement of DDE when it constitutes less than 10% of the total DDT-derived material in the eluate from the chromatographic column. It is possible that a limitation of the chemical methodology may account for the apparent difference in the way in which human beings handle recrystallized DDT and technical DDT.

No conclusion can be reached regarding the time at which equilibrium is reached in the storage of DDE. Figure 3 might be thought to suggest the establishment of equilibrium at about a year, but the number of values available for comparison is very small. In animals, it generally requires longer to establish storage equilibrium for DDE than for DDT.

Table 6.—*Variability in Fat Storage of DDT Expressed on the Basis of Concentration and Total Amount Stored*

Duration of Exposure, Mo.	Daily DDT Dosage, Mg.	No. of Men	DDT Storage in Fat: Concentration: Mean, Ppm	Concentration: Vx̄,* %	Total Amount: Mean, Gm.	Total Amount: Vx̄,* %
	0	4	8.5	18.0	0.109	14.0
5.9	3.5	5	25.2	15.9	0.354	11.8
	35	9	167.0	17.9	2.245	15.5
	0	3	11.6	24.1	0.152	26.9
11.5-12.9	3.5	4	44.0	34.1	0.613	23.2
	35	8	270.0	15.9	3.280	15 2

* Coefficient of variation of the standard error of the mean.

As an alternative to the use of concentration as a measure of DDT storage, the total amount of DDT stored per man was considered. This value was determined by multiplying the weight of the subject's body fat by the concentration of DDT in his fat. In table 6, the results of this study are shown. It is apparent from inspection of the coefficients of variation that the intergroup differences were about the same, using either DDT concentration in fat or total DDT content as a measure of the magnitude of DDT storage. The average total DDT storage for the highest dosage group after 12 months of exposure was 3.28 gm., based on measured concentration of DDT in fat and estimated total body fat. This average total storage would represent a potential DDT dosage to the average man (70 kg.) of 47 mg. per kilogram. It is unrealistic to suppose that fat would ever be metabolized rapidly enough to cause acute clinical DDT poisoning when the total available dosage is 50 mg. per kilogram or less.

In single specimens of blood taken from 4 men who had received 599 or more doses at the highest rate, DDT was found at a concentration of 1.6 to 4.2 ppm or an average of 2.8 ppm. DDE was found in these specimens at concentrations of 1.3 to 3.1 ppm or an average of 1.9 ppm. In the individual samples, DDE constituted 34 to 45% of the total DDT-derived material. Specimens of saliva collected the same day from the same 4 men contained no detectable DDT-derived material. Results were also negative for a single specimen of bile diluted with intestinal juice.

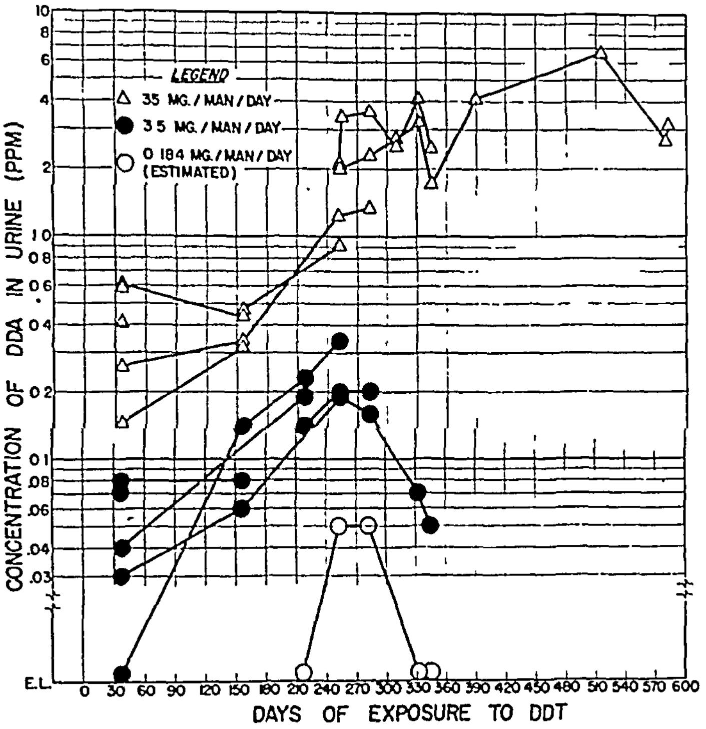

Fig. 4.—Urinary excretion of DDA by men given indicated dosage of recrystallized *p,p'*-isomer of DDT. E. L. = experimental limit, a concentration too small to be detected by the available chemical method.

Excretion of DDT-Derived Materials.—Urinary excretion of DDA is shown in figures 4 and 5. The study of urinary excretion was exploratory at first. The method for isolating DDA from urine was perfected during the course of the experiment.[8] For this reason, the early values are considered less accurate than the later ones; even so, certain conclusions are justified. The daily ingestion of 3.5 mg. or more of DDT led to the excretion of substantial amounts of DDA in about 30 days. There were no values to indicate how early excretion might be detected regularly; however, even subjects with only dietary exposure to DDT occasionally excreted DDA at concentrations that approached 0.2 ppm, indicating a distinct relation between DDT dosage and the amount of DDA excretion. The excretion of DDA also increased with the duration of DDT exposure. The highest concentration of DDA observed in a single sample was 9.6 ppm. Of particular interest was the study of 24-hour urine samples recorded in table 7. These samples show the marked variation of DDA concentration characteristic of samples collected at a single voiding. When the concentration was multiplied by volume to give total DDA content in milligrams, the variation was reduced. Thus, considering all observed values, the coefficient of variation for DDA concentration was 16.3%, whereas that for total DDA content of the same samples was only 5.4%. The variation between samples of urine from a given man taken on different days tended to be about the same as the variation between samples from different men taken on the same day. The specific gravity of urine samples tends to be inversely proportional to the volume; however, the variation in DDA concentration values for urine samples collected at a single voiding could not be decreased significantly by adjusting the values in accordance with the specific gravity of the various samples. In view of the results with 24-hour samples, this may indicate that the excretion of DDA does not parallel that of sodium chloride and other solids, which play a major role in the determination of specific gravity.

Expressed as DDT, the DDA found in the 24-hour urine samples varied from 4.8 to 9.6 mg. and averaged 6.7 mg. per sample. Thus, after storage equilibrium had been achieved, it was possible, through urinary excretion, to account for 13.6 to 27.4% or an average of 19.0% of the entire ingested dose. Figures 4 and especially 5 suggest that equilibrium of DDA excretion is reached in about a year. A specimen of feces from a man at the highest dosage level contained DDT (2.6 ppm) and DDE (2.7 ppm). Difficulty with isolating DDT-deriven material from human feces is great, especially with the acid fraction (DDA and related materials). DDA was not demonstrated, but its presence, or the presence of related material, is not excluded.

Comment

As shown in table 8, the median storage of DDT found in the volunteers before they entered the experiment corresponded well with that reported by Laug and co-workers [10] for a series of samples collected from the general population sometime before 1951. Laug and his colleagues did not distinguish DDE. The estimation of DDT reported in that paper is more comparable with the estimation of DDT in the present paper than with the estimation of DDT plus DDE. The distribution of the present values for DDT storage differs from the distribution reported by Laug in that the more recent work shows a concentration of figures near the mean and no values at all corresponding to Laug's high and low ranges. This difference in distribution may be explained by a more constant and more

TABLE 7.—*Recovery of DDA from Twenty-Four-Hour Urine Specimens from Volunteers Who Had Received DDT at the Rate of Thirty-Five Milligrams per Man per Day for Sixteen or More Months*

Group no.		3	6	6	6	6
Case no.		25	44	46	47	49
Concentration of DDA ppm	Oct. 3	2.70	7.04	1.66	2.55	3.08
	Oct. 4	3.12	2.04	6.45	0.77	2.08
	Nov. 29	...	...	...	1.06	5.90
	Nov. 30	...	...	...	2.80	5.60
	Mean	2.91	4.54	4.06	1.79	4.16
	S.E.	0.21	2.50	2.38	0.51	0.94
Concentration of DDA, $V_{\bar{x}}$,* %		7	55	59	29	23
Amount of DDT-equivalent,† mg./24 hr.	Oct. 3	7.35	7.23	8.80	6.30	6.40
	Oct. 4	6.47	6.34	9.61	4.76	5.56
	Nov. 29	...	...	...	5.39	5.65
	Nov. 30	...	...	...	7.48	5.86
	Mean	6.91	6.78	9.20	5.98	5.87
	S.E.	0.47	0.48	0.41	0.63	0.19
Amount of DDT, $V_{\bar{x}}$,* %		7	7	4	11	3

* Coefficient of variation of the standard error of the mean.

† (Mg./kg. of DDA) × (kg. of urine) × 1.26. This latter factor (the dividend obtained by dividing the molecular weight of DDT by the molecular weight of DDA) serves to convert DDA values to DDT equivalent values.

controlled use of DDT in agriculture at the present time. Earlier use of the pesticide was more sporadic and may have been less well regulated. The difference in distribution may also be related to differences in chemical method. Early unpublished studies carried out in this laboratory at about the same time as those of Laug show the same distribution and general magnitude of values as those reported by Laug. These early studies involved sufficient differences in chemical method from those now used that it is difficult to evaluate the results. Interpretation of early zero values appears especially difficult.

The concentration of DDT stored in the fat of the volunteers at apparent equilibrium after the highest dosage was almost as high as that for one man with extensive occupational exposure who showed 648 ppm of DDT and 434 ppm of DDE. The DDE stored by the volunteers constituted only an average of 16% or less of their total DDT-derived material, whereas the corresponding value for the man with occupational exposure was 40%. The difference was probably related to the duration of high exposure—18 months or less for the group and five years for the worker.

Summary and Conclusions

With full knowledge of the plan of the study and with complete freedom to withdraw at any time, 51 men volunteered to take daily, oral doses of DDT for different intervals. One-third of the men received no DDT except that in the ordinary diet; one-third received 3.5 mg. per man per day; and one-third received 35 mg. per man per day, which is about 200 times the daily rate at which an average man receives DDT from his diet. During the entire study, no volunteer complained of any symptom or showed, by the tests used, any sign of illness that did not have an easily recognized cause clearly unrelated to exposure to DDT.

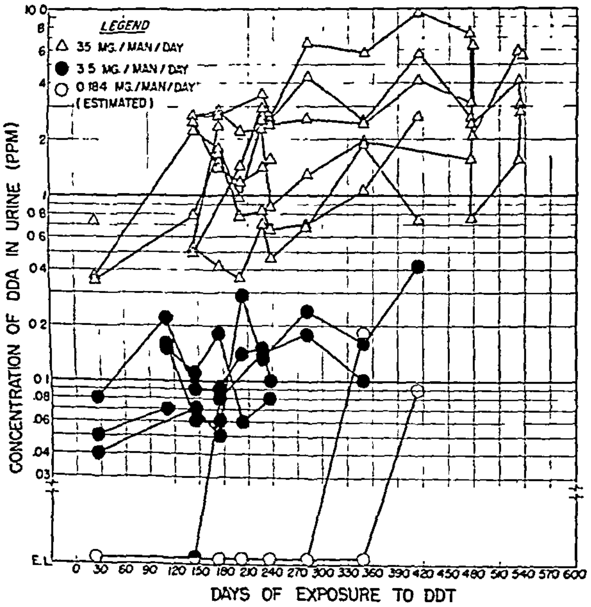

Fig. 5.—Urinary excretion of DDA by men given indicated dosage of technical DDT. E. L. = experimental limit, a concentration too small to be detected by the available chemical method.

The storage of DDT in man is proportional to dosage. There was an unexplained difference in the storage of recrystallized and of technical DDT. The pure material was stored in fat at an average concentration of 340 ppm and the technical material at an average concentration of 234 ppm after an identical dosage of 35 mg. per man per day. It appears that, at the dosages used, human males achieve maximum storage of DDT in about a year and thereafter store no more of the material despite continued intake. Men who ate DDT showed an absolute increase in the storage of DDE. No conclusion could be reached regarding the time at which equilibrium is reached in the storage of DDE. The storage of DDT and the storage of DDE show about the same relative variation (coefficient of variation) at different dosage levels, but the absolute variation is, of course, greater at higher dosages.

Table 8.—*Range of Concentration of DDT Found in Human Fat*

Range	Cases, %	
Ppm DDT	Laug Report	This Study
0.0	20	0
0.1-1.0	9	0
1.1-5.0	28	25
5.1-10.0	28	61
10.1-20.0	12	14
Over 20.0	3	0

A method for determining the concentration of DDA in urine was perfected during the course of the study. The excretion of DDA is proportional to the dosage of DDT. This makes possible an objective measurement of DDT absorption by the determination of DDA in urine and greatly expands the possibility of practical study of formulators and others who have occupational exposure to DDT. It was possible to account for about 20% of the DDT administered, in terms of DDA excreted in the urine. The results indicate that a large safety factor is associated with DDT as it now occurs in the general diet.

The chlorophenothane (DDT) capsules were supplied by R. P. Scherer Corporation, Detroit.

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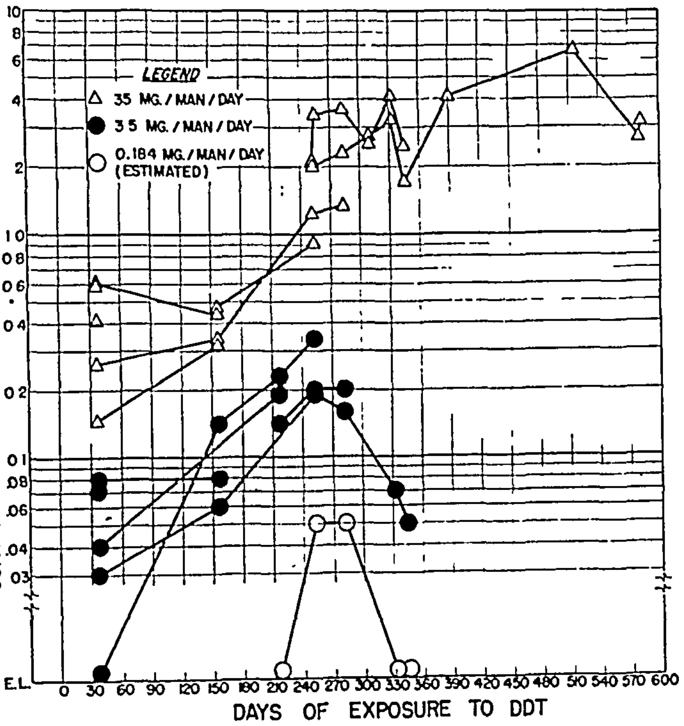
In single specimens of blood taken from 4 men who had received 599 or more doses at the highest rate, DDT was found at a concentration of 1.6 to 4.2 ppm or an average of 2.8 ppm. DDE was found in these specimens at concentrations of 1.3 to 3.1 ppm or an average of 1.9 ppm. In the individual samples, DDE constituted 34 to 45% of the total DDT-derived material. Specimens of saliva collected the same day from the same 4 men contained no detectable DDT-derived material. Results were also negative for a single specimen of bile diluted with intestinal juice.



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Excretion of DDT-Derived Materials.—Urinary excretion of DDA is shown in figures 4 and 5. The study of urinary excretion was exploratory at first. The method for isolating DDA from urine was perfected during the course of the experiment.[8] For this reason, the early values are considered less accurate than the later ones; even so, certain conclusions are justified. The daily ingestion of 3.5 mg. or more of DDT led to the excretion of substantial amounts of DDA in about 30 days. There were no values to indicate how early excretion might be detected regularly; however, even subjects with only dietary exposure to DDT occasionally excreted DDA at concentrations that approached 0.2 ppm, indicating a distinct relation between DDT dosage and the amount of DDA excretion. The excretion of DDA also increased with the duration of DDT exposure. The highest concentration of DDA observed in a single sample was 9.6 ppm. Of particular interest was the study of 24-hour urine samples recorded in table 7. These samples show the marked variation of DDA concentration characteristic of samples collected at a single voiding. When the concentration was multiplied by volume to give total DDA content in milligrams, the variation was reduced. Thus, considering all observed values, the coefficient of variation for DDA concentration was 16.3%, whereas that for total DDA content of the same samples was only 5.4%. The variation between samples of urine from a given man taken on different days tended to be about the same as the variation between samples from different men taken on the same day. The specific gravity of urine samples tends to be inversely proportional to the volume; however, the variation in DDA concentration values for urine samples collected at a single voiding could not be decreased significantly by adjusting the values in accordance with the specific gravity of the various samples. In view of the results with 24-hour samples, this may indicate that the excretion of DDA does not parallel that of sodium chloride and other solids, which play a major role in the determination of specific gravity.

Expressed as DDT, the DDA found in the 24-hour urine samples varied from 4.8 to 9.6 mg. and averaged 6.7 mg. per sample. Thus, after storage equilibrium had been achieved, it was possible, through urinary excretion, to account for 13.6 to 27.4% or an average of 19.0% of the entire ingested dose. Figures 4 and especially 5 suggest that equilibrium of DDA excretion is reached in about a year. A specimen of feces from a man at the highest dosage level contained DDT (2.6 ppm) and DDE (2.7 ppm). Difficulty with isolating DDT-deriven material from human feces is great, especially with the acid fraction (DDA and related materials). DDA was not demonstrated, but its presence, or the presence of related material, is not excluded.

Comment

As shown in table 8, the median storage of DDT found in the volunteers before they entered the experiment corresponded well with that reported by Laug and co-workers[10] for a series of samples collected from the general population sometime before 1951. Laug and his colleagues did not distinguish DDE. The estimation of DDT reported in that paper is more comparable with the estimation of DDT in the present paper than with the estimation of DDT plus DDE. The distribution of the present values for DDT storage differs from the distribution reported by Laug in that the more recent work shows a concentration of figures near the mean and no values at all corresponding to Laug's high and low ranges. This difference in distribution may be explained by a more constant and more

TABLE 7.—*Recovery of DDA from Twenty-Four-Hour Urine Specimens from Volunteers Who Had Received DDT at the Rate of Thirty-Five Milligrams per Man per Day for Sixteen or More Months*

Group no.		3	6	6	6	6
Case no.		25	44	46	47	49
Concentration of DDA ppm	Oct. 3	2.70	7.04	1.66	2.55	3.08
	Oct. 4	3.12	2.04	6.45	0.77	2.08
	Nov. 29	...	...	...	1.06	5.90
	Nov. 30	...	...	...	2.80	5.60
	Mean	2.91	4.54	4.06	1.79	4.16
	S.E.	0.21	2.50	2.38	0.51	0.94
Concentration of DDA, Vx̄,* %		7	55	59	29	23
Amount of DDT-equivalent,† mg./24 hr.	Oct. 3	7.35	7.23	8.80	6.30	6.40
	Oct. 4	6.47	6.34	9.61	4.76	5.56
	Nov. 29	...	...	...	5.39	5.65
	Nov. 30	...	...	...	7.48	5.86
	Mean	6.91	6.78	9.20	5.98	5.87
	S.E.	0.47	0.48	0.41	0.63	0.19
Amount of DDT, Vx̄,* %		7	7	4	11	3

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* Coefficient of variation of the standard error of the mean.

† (Mg./kg. of DDA) × (kg. of urine) × 1.26. This latter factor (the dividend obtained by dividing the molecular weight of DDT by the molecular weight of DDA) serves to convert DDA values to DDT equivalent values.

THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

None of us had to register to vote, and perhaps there are some who did not. None of us has to vote on Nov. 6, either, and there are some who will not. None of us even has to vote for all the offices on the ballot, and election results always show that voters skip over many offices. No, there is no one forcing us to register, no one herding us to the polls, and no one compelling us to fill out the complete ballot. Our voting process is entirely voluntary, with the choice of registering and voting up to the individual. We might even say that the right-to-stay-at-home on election day is a privilege we all have. But all privileges are not always advantageous to us and to society, and certainly a decision to ignore voting can be political suicide from the standpoint of the individual, the community, and the nation.

Our whole system of representative government rests on the basic principle that election decisions should be made by all the people eligible to vote. If we fail to vote, we undermine that system of government by destroying its basic principle. If there is a more valuable right of an American citizen than the right to vote, I do not know what it could be. It is a right that must be exercised completely and thoughtfully, beginning with registration and following through to voting for the last candidate on the ballot.

Those of us who have registered have taken the first big step, and we cannot afford to stay home and thus lose our vote like so many have already done by failing to register. The government we have is ours, and the government we are going to get on Nov. 6 is to be ours. That is the way we want it, and that is the way it will stay as long as we conscientiously exercise our right of franchise. The idea that "poor government and bad officials are elected by good citizens who do not vote" is old, but it bears repeating and remembering.

Now is the time to make our decisions on the candidates. Study them and the issues so you will be prepared to vote for those you think will serve your community, state, and nation best. Last-minute decisions in the polling booth are not fair to the candidates, and they are hit-or-miss conclusions. Those we elect on Nov. 6 will be managing our affairs at all levels and introducing legislation for the next few years. After election day it will be too late to complain that we did not know a certain defeated candidate believed as we do. There are only a few days left to learn the candidates and the issues, but, if we are to vote intelligently, it is our duty to know and to decide before going to the polls.

Registration this year is heartening, and there is reason to believe the 61,500,000 votes of 1952, or the 62.7% of the eligible voters, will be surpassed in the coming election. The time we spend learning about the candidates and issues—local, state, and national—is as important as the actual casting of a ballot. There is still time to review records, policies, and pledges and to appraise the candidates. Do not put it off; the time is too short. And do not stop with an analysis of just the presidential, senatorial, and congressional races. Decide on candidates for every state and local office lest you be tempted to vote for someone only because he has a familiar name or he belongs to your party. Every elective office is an important position, and it deserves the attention of all responsible voters.

After you have made your choices, do not fail to vote. Many contests have been decided by a single vote. Our history—past and present—is full of such examples. My own state of California was admitted to the Union by one vote, and I have seen many districts in the nation carried by a single vote. I cast my vote knowing that it can elect my candidate or defeat an opponent. I cast it realizing that my candidate deserves it and needs it if he is to win. One vote can be a powerful force. It wins or loses battles, and we do not have to turn the calendar back too many months to prove dramatically that it does happen.

You undoubtedly have strong opinions about the issues and the candidates, but what good will these be if you fail to exercise your franchise? Your voice will be heard clearly if you speak at the polls in behalf of the issues and personalities you favor.

Doctor, make yourself an appointment to vote on Nov. 6, and do not fail to keep it. You and your government could be a heavy loser if you stay home.

Dwight H. Murray, M.D.,
Napa, Calif.

ORGANIZATION SECTION

LET'S KEEP THE DOOR OPEN

George F. Lull, M.D., Chicago

When the American Legion and the American Medical Association agree—as they already do on many principles and in many areas of activity—they should cooperate to the fullest possible extent, not just for their mutual benefit but for the benefit of all Americans. On the other hand, if and when they disagree on certain points, they must do so calmly, reasonably, and with respect for one another's motives. After all, differences of opinion, and the right to express those opinions, are important ingredients in the democracy to which both groups are dedicated.

That is the essence of my main message. Why does the A. M. A. consider it good policy to repeat and reemphasize that message whenever possible? What has happened in relations between the Legion and the A. M. A. to make such a message necessary? For the benefit of those who may not be familiar with this subject, I shall sketch very briefly the background of the past three years. Also, I would like to report some of the most recent developments bearing on the situation.

Recent Developments

For about 20 years, until June, 1953, the Legion and the A. M. A. had a friendly relationship, in which they exchanged views, cooperated on certain projects, and shared many common objectives. That relationship was based on the fact that both organizations are influential, patriotic groups dedicated to the American way of life and opposed to any trends or influences that would undermine the foundations of our national vitality. Fortunately, that basis for cooperation still exists.

However, the calm water became somewhat choppy after the 1953 Annual Meeting of the A. M. A. At that time the House of Delegates adopted the Association's present policy concerning the federal government's responsibility for the hospital and medical care of veterans with non-service-connected disabilities. That policy—and I want to emphasize this—that policy in no way suggested any change or limitation in the Veterans Administration's program of care for veterans with service-connected disabilities. The A. M. A. heartily supports that program, which is a definite national obligation to veterans who are ill or disabled as a result of their military service. The present A. M. A. policy also does not involve wartime veterans with non-service-connected tuberculosis or neuropsychiatric disorders, whenever local facilities are unavailable. The policy simply recommends that the remaining non-service-connected disabilities—the so-called general medical and surgical conditions that have no relation to military service—should become the responsibility of the individual veteran and his community, instead of the federal government.

For more than a year after the A. M. A. adopted that policy, relations with the Legion were, to put it mildly, not exactly convivial. Most physicians were amazed at some of the extreme and bitter charges made against the medical profession by a few Legion officials. We can only conclude that some of the national and state Legion leaders who were in office at the time either misunderstood or misinterpreted the A. M. A. policy. At any rate, there was a welcome change of atmosphere after the 1954 national convention of the American Legion. The new national commander, Seaborn P. Collins, addressed the A. M. A. House of Delegates later that year at the Clinical Meeting in Miami, Fla. He urged that the controversy over veterans' medical care be removed from the area of name-calling and propaganda, and he emphasized the point that "we are citizens first, and doctors and veterans second."

Suggesting establishment of a liaison arrangement to help work out a better mutual understanding, Mr. Collins told the A. M. A. House of Delegates, "If our two groups approach the subject of medical care for veterans in this sincere, honest and reasonable fashion, I believe that we can resolve our differences, or at least achieve an understanding of each other's position which will permit us to continue to collaborate and cooperate in those fields where we do agree."

As a result of that suggestion, both the Legion and the A. M. A. appointed liaison committees to explore possible areas of agreement. Those committees met several times during 1955 and the early part of this year. They reached agreement on a number of points, but they were far apart on others. However, the important thing is that they got together in an atmosphere of reason, mutual respect, and friendly give-and-take across the conference table. And Dr. Elmer Hess, immediate past-president of the A. M. A., in his term-end report to the House of Delegates in Chicago in June, paid particular tribute to the cooperative spirit of Mr. Collins and Governor George Craig of Indiana, another past-commander of the Legion.

The A. M. A. liaison committee, after presenting its report to the Board of Trustees, was discharged from further duty. The issues in question have been referred back to the Committee on Federal Medical Services of the Council on Medical Service, which will continue its studies in the field of veterans' medical care. At the Chicago meeting, the A. M. A. House of Delegates adopted a report by the Committee on Federal Medical Services that included the following statements:

> The Committee is of the opinion that the American Medical Association and the American Legion should continue to cooperate in an effort to provide the finest medical care for all segments of the American public, with special emphasis on the

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Secretary-General Manager of the American Medical Association.

Read before the Arkansas Department of the American Legion, El Dorado, Ark., July 20, 1956.

obligations of a grateful nation toward those who have suffered disability as a result of military service. It is the further recommendation of the Committee that both organizations should join in aggressively seeking an adequate program of prevention and treatment of mental disorders.

Another point on which the two organizations have had differences of opinion in the past is the practice of establishing a "presumption" of service connection for veterans' disabilities by legislative action rather than by scientific medical examination. Under this practice, which already includes about 30 specific disabilities, a condition is automatically assumed to be service-connected if it occurs within a certain length of time after discharge from service. This, in effect, is simply an indirect method of increasing the VA load of patients with non-service-connected disabilities. The A. M. A. believes, and has so testified many times before congressional committees, that each case should be determined on an individual basis, after sound, careful, medical examination. It holds that it is medically illogical and economically unsound to pass laws that decree that a disability is automatically classified as service-connected simply because it occurs within one, or two, or three years after military discharge. The result of this trend could well be that Congress would declare all veterans' ailments to be service-connected. It has been encouraging to note that in this session of the 84th Congress the Legion has actively supported only one of the most recent bills proposing still more presumptions of service connection. That bill is H. R. 1618, which involves multiple sclerosis and the chronic functional psychoses.

That, as far as my knowledge goes, is the present situation. The really important point, in my opinion, is the fact that for almost two years now the Legion and the A. M. A. have kept the discussions of these issues on a high level. During that period of time, the problem has been removed from the area of name-calling and propaganda, charges and countercharges, smear tactics and emotionalism. I am sure that I express the hope of the vast majority of both physicians and legionnaires when I say, "Let's keep it that way."

Areas of Agreement and Cooperation

The groups have too much in common—as patriotic Americans, as fellow veterans, as staunch defenders of freedom and democracy, and as partners in several specific projects of mutual interest—to allow differences of opinion over one issue to threaten their fundamental unity of purpose. Whether they ever agree on all aspects of the veterans' medical care problem, they should continue to work together in those areas where their joint efforts will constitute a service to our country. After all, every year in this country thousands of couples celebrate their golden wedding anniversaries. In the vast majority of cases, we would be rather "pollyanna" and unrealistic if we assumed that those couples never had an argument. Nevertheless, whether they argued over in-laws, money, or the husband's cigar smoking, they did not allow such side issues to disrupt their basic unity. They might have not been completely enchanted with one another every hour of every day, but they did not let temporary irritations destroy something far more important. The Legion and the A. M. A., of course, could hardly be described as an elderly married couple, but I think the basic analogy holds true. By keeping differences in proper perspective, they can preserve a working relationship and a common devotion to American ideals that will be of benefit to our nation.

For example, in the broad field of ideology the Legion and the A. M. A. stand together as enemies of communism, socialism, fascism, or any other political, social, and economic philosophy that is contrary to American tradition. The Legion was one of the medical profession's earliest and most helpful allies in its campaign against national compulsory health insurance just a few years ago. The A. M. A. for the past five or six years has contributed annually to help support the All-American Conference to Combat Communism, a project in which the Legion also has been interested. Both organizations are increasing their efforts to develop a positive understanding of Americanism and to urge a wider, more vigorous participation in the duties of citizenship. Both the Legion and the A. M. A. have affirmed and reaffirmed their support of the general principles contained in the so-called Bricker amendment. The purpose of that proposed amendment to the Constitution is to protect the nation and the individual states from unwanted legislation that might be imposed through treaties or executive agreements with foreign countries.

For many years, to mention a specific project of a different kind, the Legion and the A. M. A. have been working together in the field of maternal and child health. In fact, Dr. Garland Murphy of El Dorado, Ark., vice-chairman of the Legion's child welfare commission, is the Legion's representative on the Committee on Maternal and Child Care of the A. M. A. Council on Medical Service. Both the Legion and the A. M. A. actively supported the Mental Health Study Act of 1955, which was passed by Congress last year without a dissenting vote. Under that law, an intensive three-year study is now under way by the Joint Commission on Mental Illness and Health, an organization sponsored by the A. M. A., along with about 20 other groups interested in that field. This is another area where the Legion and the A. M. A. can do much to help solve a major national health problem, for the benefit of veterans and nonveterans alike. There are many other projects, subjects, and ideas on which the American Legion and the American Medical Association already cooperate, already agree, or can do so in the future. Let's keep the door open—by keeping our heads.

MEDICAL CIVIL DEFENSE CONFERENCE

The County Medical Societies Civil Defense Organization will hold its seventh conference on Nov. 10-11, 1956, in Chicago at the Morrison Hotel. The Council on National Defense of the American Medical Association sponsors this yearly conference, which is designed to help local medical and health personnel plan for their roles in civil defense. The conference program, this year, is specifically planned to acquaint individuals at the local medical and health group level with practical information concerning responsibilities, preparation, and coordination of medical and health civil defense activities. Individuals desiring additional information on this conference are requested to contact Mr. Frank W. Barton, Secretary, Council on National Defense, American Medical Association, 535 N. Dearborn St., Chicago 10.

PROGRAM
SATURDAY MORNING—NOV. 10, 1956
COTILLION ROOM

8:00-9:00 **Registration**

9:00-9:05 **Call to Order**
Max L. Lichter, M.D., Member, Committee on Civil Defense, Council on National Defense, A. M. A., Detroit.

9:05-9:15 **Address of Welcome**
Harold C. Lueth, M.D., Chairman, Committee on Civil Defense, Council on National Defense, A. M. A., Evanston, Ill.

9:15-10:00 **A Critical Analysis and Evaluation of Civil Defense**
Honorable Chet Holifield, U.S. Congressman, 19th District of California, Chairman, Sub-Committee on Military Operations, Committee on Government Operations.

10:00-12:00 **How to Plan for Disaster—Panel Discussion**
Moderator—Charles P. Anderson, M.D., Deputy Commissioner, Medical Services, Department of Health, Detroit.

- (a) Casualty Estimates in Nuclear Warfare
  Lieut. Col. Arthur Steer, M.C., U. S. A., Deputy Commandant, Walter Reed Army Institute of Research, Washington, D. C.
- (b) Current Planning Concepts
  M. M. Van Sandt, M.D., Director, Medical Care Division, Health Office, Federal Civil Defense Administration, Battle Creek, Mich.
- (c) Management and Care of Mass Casualties
  Col. Joseph R. Shaeffer, M.C., U. S. A., Chief, Department of Atomic Casualties Studies, Walter Reed Army Institute of Research, Washington, D. C.
- (d) Hospital Planning for Disaster
  Jacques Cousin, Director, Oakwood Hospital, Dearborn, Mich.

12:00 Luncheon—Embassy Room

SATURDAY AFTERNOON—NOV. 10, 1956
COTILLION ROOM

2:00-5:00 **Workshop Session—CPX Operation (Paper Logistical Exercise)**
Presiding—C. P. Anderson, M.D.
The entire afternoon session will be devoted to group CPX sessions led by representatives of the Federal Civil Defense Administration. Conference participants will be divided into three working groups.

5:00 **Adjournment**

6:15-7:15 **Social Hour—Embassy Room**

SUNDAY MORNING—NOV. 11, 1956
COTILLION ROOM

9:00-10:30 **Reports of Workshop Sessions**
Presiding—Harold C. Lueth, M.D.

10:30-12:00 **Planning for Support—Panel Discussion**
Moderator—James H. Lade, M.D., Director, Office of Medical Defense, Department of Health, State of New York, Albany.

- (a) Resources Evaluation
  C. P. Anderson, M.D.
- (b) Federal Supplemental Support
  John M. Whitney, M.D., Director, Health Office, Federal Civil Defense Administration, Battle Creek, Mich.
- (c) Support Areas
  Frank F. Schade, M.D., Chief of Medical and Health Section of Los Angeles County and Cities Civil Defense Planning Board, Los Angeles.

12:00 **Luncheon—Embassy Room**
Mass Feeding and Integration of Services
Mrs. Kathryn G. Gasker, Executive Secretary, Disaster-Relief Committee, Academy of Medicine of Cleveland.

SUNDAY AFTERNOON—NOV. 11, 1956

2:00-3:30 **Mental Health Needs in Civil Defense and Disaster Planning—Symposium**
Ozro T. Woods, M.D., Mental Hygiene Consultant, Federal Civil Defense Administration, Dallas, Texas.
Calvin S. Drayer, M.D., Chairman, Committee on Civil Defense, American Psychiatric Association, Philadelphia.
Col. Albert J. Glass, M.C., U. S. A., Chief, Department of Neuropsychiatry, Walter Reed Army Hospital, Washington, D. C.

3:30-3:45 **The A. M. A. Council on National Defense**
Mr. Frank W. Barton, Secretary, Council on National Defense, A. M. A.

3:45-4:15 **Business Session—Adjournment**
Max L. Lichter, M.D.

PLAN HAWAIIAN TRIP AFTER SEATTLE MEETING

Physicians and their wives planning to attend the A.M.A. Clinical Session in Seattle, Nov. 27-30, are invited to take a Hawaiian vacation after the meeting. Ralph W. Neill, executive secretary of the Washington State Medical Association, has made arrangements for two different air cruises to Hawaii, direct from Seattle. Cruise highlights include air fare, accommodations at first-class hotels in Honolulu, sightseeing to the various islands, a yacht cruise of Pearl Harbor, a native "luau" and the services of experienced travel representatives. Details may be obtained from Mr. Neill, Washington State Medical Association, 1309 Seventh Ave., Seattle 1.

MEDICAL NEWS

ALABAMA

Surgeons Meeting.—The annual meeting of the Alabama division, International College of Surgeons, will be held at the Druid City Hospital, Tuscaloosa, Oct. 31. The medical profession is invited.

CALIFORNIA

Grant for Mental Health Research.—A $250,000 grant will be made by the Ford Foundation to Mount Sinai Hospital and Clinic (8712 Beverly Blvd., Los Angeles) for a portion of its mental health research program. Mount Sinai Hospital recently opened its 34-bed psychiatric inpatient department under direction of Dr. Steven D. Schwartz, chief of inpatient service of the department of psychiatry, assistant clinical professor in the department of nervous and mental diseases, College of Medical Evangelists, Los Angeles, and attending psychiatrist and neurologist at Los Angeles County Hospital (Medical Unit). The complete psychiatric program at Mount Sinai Hospital is directed by Dr. Franz Alexander, clinical professor of psychiatry at the University of Southern California School of Medicine, Los Angeles. Dr. Richard E. Renneker, formerly with the Chicago Institute of Psychoanalysis, was scheduled to join the staff in August as chief of outpatient service.

COLORADO

State Medical Election.—Officers of the Colorado State Medical Society include Dr. George R. Buck, Denver, president; Dr. Gatewood C. Milligan, Englewood, president-elect; Dr. C. Walter Metz, Denver, vice-president; Dr. James M. Perkins, Denver, constitutional secretary (three years); and Dr. William C. Service, Colorado Springs, treasurer (three years).

CONNECTICUT

Society News.—The Connecticut State Medical Society is planning to sponsor health exhibits at about 20 fairs this fall. The project, now in its fifth year, is conducted by county committees of the women's auxiliary in cooperation with the society's committee on rural health.

Fulbright Fellow.—Dr. David Weinman II, associate professor of microbiology at Yale University School of Medicine, New Haven, has been granted a Fulbright fellowship that will enable him to conduct research at Makerere College in Kampala, Uganda, East Africa. Dr. Weinman participated in the Harvard expedition to Peru in 1937 and the Harvard-American Foundation for Tropical Medicine expedition to Liberia in 1944. He has been a member of the Yale faculty since 1948.

State Aid to Nursing Education.—The Connecticut State Board of Examiners for Nursing has announced that 326 awards averaging $215 each were given to nursing students during the past year. The awards, totaling $70,000, were distributed under the provisions of section 1692C, chapter 213 of the Connecticut statutes, which provides "for a program of financial assistance and awards for nursing education in any duly accredited institution of learning in Connecticut." To be eligible for these awards a student nurse must have been a resident of the state for four years immediately before receiving the award and must agree to apply for a license as a nurse in Connecticut and to practice nursing in Connecticut immediately on graduation. The awards, according to the statute, "Shall not exceed the tuition charged by the institution together with the amount of educational fees, books, uniforms, board, and lodging."

Personal.—The University of Chicago recently conferred on Dr. John Rodman Paul, professor of preventive medicine, Yale University School of Medicine, New Haven, Conn., the honorary degree of doctor of science. The citation read, in part: "A meticulous investigator, whose fundamental studies have made valuable contributions to our understanding of the etiology, epidemiology, and control of a number of important contagious diseases."——Dr. John P. Bachman, who completed 30 years of service with the U. S. Army Medical Department in May, thereafter became the medical director of the Connecticut State Welfare Department, succeeding Dr. Harold F. Pierce, who became chief medical consultant in the department. Dr. Bachman will act as liaison with the Connecticut State Medical Society and the Connecticut Hospital Association and will administer those functions of the state welfare department concerned with the purchase of medical and hospital care.

DISTRICT OF COLUMBIA

Personal.—Dr. M. Wharton Young, professor of anatomy at Howard University College of Medicine, Washington, D. C., was appointed visiting professor of neuroanatomy at the Chicago Medical School for the summer quarter. Dr. Young was Fulbright Professor of Anatomy at Chiba University of Medicine in Japan in 1953.——At the commencement exercises June 3, Boston University bestowed the honorary degree of doctor of humane letters on Dr. Martha May Eliot, chief of the children's bureau, United States Department of Health, Education, and Welfare, Washington, D. C. Dr. Eliot has served as United States representative to the executive board of the United Nations Children's Fund since 1952 and was assistant director general of the World Health Organization, 1949-1951.——Dr. Jack Masur, assistant surgeon general and chief, Bureau of Medical Services, U. S. Public Health Service, delivered the annual Alphonse M. Schwitalla Lecture in hospital administration, sponsored by the department of hospital administration, at Firmin Desloge Hospital, St. Louis, May 15. His subject was "The Hospital Administrator and Patient Care." The lecture is given annually in honor of the Rev. Alphonse M. Schwitalla, president emeritus of the Catholic Hospital Association of the United States and Canada.——Dr. Mark S. Blumberg, formerly acting chief of the health conservation section of the U. S. Public Health Service in Washington, D. C., has joined the staff of Stanford Research Institute, Menlo Park, Calif., as an associate operations analyst in the economics division. Subjects Dr. Blumberg will consider in his new assignment include phases of health screening, industrial medicine, hospital planning, care of disaster casualties, medical education, and motor vehicle accident prevention.

FLORIDA

Course in Vectorcardiography.—A course in vectorcardiography will be given evenings at Mount Sinai Hospital of Greater Miami, Miami Beach, Nov. 5-9, by Dr. Arthur Girshman of New York City. Information may be obtained from the Medical Secretary, Mount Sinai Hospital, 4300 Alton Rd., Miami Beach, Fla.

Faculty Research Award.—The Chicago Medical School announces that, beginning with the ensuing academic year, a $1,000 award for research in medical and allied fields will be presented annually to a "promising faculty member" who has been recommended by the faculty research committee with final approval by the faculty council and board of trustees. The award is to be known as the Board of Trustees Faculty Research award.

Carlson Memorial Services.—Memorial services for Dr. Anton J. Carlson of the University of Chicago, who died Sept. 2, will be held in Pathology 117, Auditorium of Billings Hospital, 950 E. 59th St., Nov. 3, 2 p. m. Speakers will include Chancellor Lawrence A. Kimpton; John O. Hutchens, Ph.D., professor and chairman of the department of physiology; and Dr. Lester R. Dragstedt, Thomas D. Jones Professor and chairman of the department of surgery, University of Chicago School of Medicine, who will deliver the principal address.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

ILLINOIS

Chicago

DeLee Lecture.—The 1956 Solomon Theron DeLee Lecture was delivered at the Albert Merritt Billings Hospital, Oct. 10, by Dr. Hans L. Kottmeier, associate professor, Royal Karolinska Institute, Stockholm, Sweden, on "The Treatment of Uterine Carcinoma at the Radiumhemmet."

Schiller Memorial Fund.—The Alfred A. Schiller Memorial Fund, which will provide an annual lectureship, is being established at the University of Illinois College of Medicine in honor of Dr. Schiller, assistant professor of physiology, who died April 21, 1955. Contributions to the fund may be sent in care of Dr. George E. Wakerlin, 1853 W. Polk St., Chicago 12.

Study of Combined Premedical and Medical Education.—Northwestern University Medical School has received a three-year $75,000 grant from the John and Mary Markle Foundation for study of a program to combine premedical and medical education. According to Dr. Richard H. Young, dean, a portion of a recent $300,000 grant from the Commonwealth Fund also will be used to support the study. The study, which will be conducted jointly by faculty members of the medical school, the college of liberal arts, and the graduate school, will attempt to provide one continuous program of education in basic sciences, humanities, and medicine, so that students would begin the new course on graduation from high school and, after seven or eight years, finish with the degree of doctor of medicine. Two problems to be solved in setting up the program will be (1) designing the courses so that a student can logically branch out into other fields allied to medicine if he desires to drop his training to be a physician and (2) designing the program so that graduates from other liberal arts colleges may enter the medical program at Northwestern.

Personal.—Dr. Harold S. Feinhandler, clinical associate in ophthalmology at the Chicago Medical School, has been promoted to the rank of associate on the Mount Sinai Hospital staff, which is affiliated with the school as a teaching hospital.—Dr. Samuel M. Feinberg, professor of medicine, Northwestern University Medical School, spoke at Meharry Medical College, Nashville, Tenn., June 5, at the celebration of the 80th anniversary of the founding of the college. His subject was "Allergy: 1956 Inven- ory."—Dr. Albert Dorfman, associate professor of pediatrics, niversity of Chicago School of Medicine, recently lectured at e first International Symposium on Rheumatic Fever, presented by the National Institute of Cardiology, the Mexican Society of Cardiology, and the Sociedad de Internos y Becarios del Instituto Nacional de Cardiologia, in Mexico City. His topics were "Ideas on the Etiology of Rheumatic Fever" and "The Metabolism of Mucopolysaccharides."—At the invitation of the Ministry of Education of Czechoslovakia, Dr. John F. Pick presented the guest paper, "The Meaning of the Human Face," at the first International Congress of Plastic Surgeons in Prague, Czechoslovakia, Sept. 27-29.—Dr. Frederick Plotke, chief, Public Health Service, Illinois Department of Public Welfare, has been appointed assistant professor of preventive medicine and public health at the Stritch School of Medicine of Loyola University.—At the 10th annual conference in Augusta, Ga., the Association for Physical and Mental Rehabilitation bestowed the John E. Davis award on Dr. Louis B. Newman, chief, physical medicine and rehabilitation service, Veterans Administration Research Hospital, for "distinguished leadership and outstanding service in the field of physical medicine and rehabilitation."

LOUISIANA

Society News.—Recently elected officers of the Louisiana Pathology Society include Dr. Rudolph J. Muelling Jr., New Orleans, president; Dr. Ulysses H. Stoer, Shreveport, La., vice-president; and Dr. Ralph M. Hartwell, New Orleans, secretary-treasurer.

Listeriosis in An Infant.—According to the U. S. Public Health Service, Dr. Joseph D. Martin, Louisiana Department of Health, has reported a case of listeriosis in a 2-week-old infant, who became ill with a temperature of 103 F (39.4 C). Examination revealed a slight infection of the eyes, conjunctivitis, and inflammation of the posterior pharynx; later the infant began to have tonic contractions. There was mild rhinorrhea and reddening and mild bulging of the tympanic membrane of the right ear with some exudate. The white blood cell count was 13,900 per cubic millimeter; the spinal fluid was cloudy, containing 3,280 cells. Listeria monocytogenes was cultured from spinal fluid obtained three days after the onset of illness. Gram-positive diplococci were cultured from the ear exudate, but L. monocytogenes was not found. Cultures of cervical exudate from the mother were negative. The sources of the infection had not yet been identified.

MASSACHUSETTS

Visiting Lecturer in Dental Medicine.—Dr. Bengt Olof Engfeldt, professor of pathology at Uppsala University, Sweden, has been named a visiting lecturer in the Harvard School of Dental Medicine in Boston. Dr. Engfeldt, who studies the life cycles of bone tissue and the diseases and injuries affecting its normal construction and reconstruction, is particularly concerned with the way in which bone tissue retains radioactivity and the effect this radiation may have on surrounding tissue, including the bone marrow. Dr. Engfeldt has served as visiting research worker at the School of Anatomy, Cambridge University, and the Biophysical Unit of King's College, London, and as associate professor of pathology at his alma mater, the Karolinska Institute at Stockholm University.

MINNESOTA

Personal.—Dr. William L. Benedict of Rochester, executive secretary-treasurer of the American Academy of Ophthalmology and Otolaryngology, has been appointed to the National Advisory Neurological Diseases and Blindness Council for a term of four years. He thus becomes one of 12 members of the council who advise the surgeon general on the research program of the National Institute of Neurological Diseases and Blindness.

McGraw Lecture.—The recent annual McGraw Lecture was delivered by Dr. James T. Priestley, professor of surgery, University of Minnesota Graduate School, Minneapolis-Rochester, whose topic was "Hyperfunctioning Lesions of the Adrenal Gland." The McGraw Lectureship was established in 1948 by the Detroit Surgical Association in honor of Dr. Theodore A. McGraw, a founder and first professor of surgery at the Detroit College of Medicine, now Wayne University College of Medicine, Detroit. The McGraw medal was awarded to Dr. Priestley and to Dr. Charles G. Johnston, Detroit, at the meeting.

Fifty-Year Club.—At the annual banquet of the Minnesota State Medical Association in Rochester, the following physicians were made members of the "50 Club": John F. Hendrickson, Gilbert L. Doxey, Ette L. Meyer, and Frederick C. Rodda, all of Minneapolis; Robert M. Burns, Harold J. Rothschild, O. William Holcomb, Andrew W. Hilger, and Ernest T. F. Richards, all of St. Paul; Samuel J. Hillis, Bradenton, Fla., and Henry G. Collie, St. Petersburg, Fla., both formerly of St. Paul; Edward L. Tuohy, Santa Barbara, Calif., formerly of Duluth; Winslow C. Chambers, Blue Earth; Arthur W. Ide, White Bear Lake; Archibald W. Graham, Chisholm; John W. Helland, Spring Grove; Johannes C. Jacobs, Willman; Herman Linde, Cyrus; Henry E. Nelson, Crookston; Oliver M. Porter, Atwater; Ludwig L. Sogge, Windom; Joseph D. Waller, Pine City; and Alexander M. Watson, Royalton.

MISSOURI

Hospital News.—In connection with their centennial festivities, the Sisters of Mercy of St. Louis have established a historical museum in a room attached to their convent at St. John's Hospital, 307 S. Euclid Ave., St. Louis. Dr. Alphonse McMahon is the hospital's chief of staff.

NEW YORK

Society News.—At the first meeting of the newly organized Westchester chapter of the American Federation for Clinical Research, Sept. 24 at White Plains Hospital, Dr. Dennison Young was elected president; Dr. Charles A. Bertrand, vice-president; and Dr. Alfred S. Dooneief, secretary-treasurer.

New Position at Albany College.—Dr. William P. Nelson III, chief of medical service, Veterans Administration Hospital, Albany, and assistant professor of medicine, Albany Medical College, has been named to the new administrative position of assistant dean and assistant director of postgraduate medical education at the medical college. He will collaborate with the director of postgraduate medical education, Dr. Frank M. Woolsey Jr., and be concerned with such undergraduate problems as admissions, health, curriculum, counseling, and internships and will also work in teaching and research and in the development of close rapport between Albany Hospital and the Veterans Administration Hospital.

Promoted to Professorships.—The State University of New York College of Medicine at Syracuse has announced the promotion to full professorship of Dr. Harry A. Feldman, chief, section of preventive medicine, and Drs. Paul A. Bunn and Eugene L. Lozner, department of medicine. Dr. Bunn, who came to the college of medicine as associate professor of medicine in 1947, has been consultant to the tuberculosis division of the U. S. Public Health Service and a member of the committee on research and education of the American Trudeau Society. He was president of the New York State Trudeau Society, 1953-1954. He has been affiliated with University Hospitals in Cleveland, the University of Michigan hospital in Ann Arbor, Cornell University hospital in New York, and the Veterans Administration. Dr. Feldman, who became associate professor of medicine at the college of medicine in January, 1949, was appointed chief of the section of preventive medicine when it was established in November, 1955. He had served as a research fellow at George Washington University School of Medicine, Washington, D. C., and at Harvard Medical School, Boston. He entered the Medical Corps of the Army in 1942 and, after separation from the service, was appointed a Senior Fellow in Virus Diseases of the National Research Council, conducting research in viral diseases of childhood at the Children's Hospital Research Foundation, Cincinnati. Dr. Lozner, who came to the college of medicine as associate professor in October, 1947, served as director of clinical laboratories at Syracuse Memorial Hospital from 1948 to 1952 and since 1948 has held the same position at University Hospital. For three years he has been chairman of the blood bank committee of the Onondaga County Medical Society. From 1941 to 1946 Dr. Lozner was on active duty in the U. S. Navy, and from 1946 to 1947 he was instructor in medicine at Harvard Medical School, Boston.

New York City

Study of Pancreatitis.—The University Hospital of the New York University–Bellevue Medical Center has received a John A. Hartford Foundation grant of $159,000 for a comprehensive study of pancreatitis in all its stages. Dr. J. William Hinton, director of the University Hospital department of surgery, will direct the project and will be assisted by Dr. L. Corsan Reid, professor of research surgery, New York University Post-Graduate Medical School, and Drs. George Mixter and Robert B. Pfeffer, who hold the rank of assistant attendingmen at University Hospital.

Course on Office Proctology.—Dr. Robert Turell and staff will give a course on office proctology Nov. 12-13 at the Mount Sinai Hospital in affiliation with Columbia University. The course, designed to acquaint the clinician with the important proctologic conditions that lend themselves to office diagnosis and treatment, will include demonstration of all diagnostic and various therapeutic procedures. The course (fee $50) will be repeated Feb. 18-19, 1957. For information address the Registrar for Postgraduate Medical Instruction, Mount Sinai Hospital, Fifth Avenue and 100th Street, New York 29.

Medical Art Exhibit.—A collection entitled "Ars Medica," including 85 rare pieces bearing on the teaching and practice of medicine, is on exhibit during October at the New York Academy of Medicine, 2 E. 103rd St. The exhibit is open to the public from 9:30 a. m. to 5 p. m. daily except Sundays (admission free). Among the prints are the Vesalius "Ninth Plate of Muscles"; Rembrandt's "Portrait of Dr. Ephraim Bonus"; Bellini's "Visit to the Plague Patient"; Eakins' original engraving of "The Gross Clinic"; Bosse's engraving of "The Confinement"; Winslow Homer's Civil War portrayal of the "Surgeon at Work During an Engagement"; Hogarth's "The Company of Undertakers"; and Toulouse-Lautrec's lithograph of the sick French premier Carnot.

Meeting of General Practice Group.—The seventh annual scientific assembly of the Nassau County chapter of the American Academy of General Practice will be held at the Garden City Hotel, Garden City, Nov. 7. The program, beginning at 10 a. m., will include the following presentations:

Hazards in Treatment of Acute Myocardial Infarction, Henry I. Russek, Staten Island.
Infectious Diseases: Basic Considerations with Respect to Their Pathogenesis, Diagnosis, and Management, Theodore E. Woodward, Baltimore.
Use of Antibiotics in Treatment of Infections, Ivan L. Bennett Jr., Baltimore.
Advances in Cardiac Surgery, Charles P. Bailey, Philadelphia.
Purpura, William Dameshek, Boston.
Roles of General Practitioner and Ophthalmologist, Adolph W. Vogel, Philadelphia.

Psychosomatic Forum.—The Psychosomatic Forum of New York City (American Psychosomatic Society) will meet in the Blumenthal Auditorium of Mount Sinai Hospital (Atran Laboratory Building entrance, Fifth Ave.), Oct. 30, 8:30 p. m. Dr. Robert Dickes, associate professor of psychiatry, State University of New York College of Medicine at New York City, Brooklyn, will serve as chairman for the following panel on "The Tranquilizers":

Psychiatric Implications of Tranquilizing Drugs, Paul H. Hoch, New York City.
Some Pharmacological Aspects of the Newer Psychiatric Agents, Murray E. Jarvik, New York City.
Psychodynamic Action of Chlorpromazine and Reserpine, Mortimer Ostow and Nathan S. Kline, New York City.

A collation will follow the program, which is open to all interested persons.

Dedicate Chair of Dermatology.—In ceremonies in the Bellevue Psychiatric Hospital Amphitheatre, the George Miller MacKee Chair of Dermatology and Syphilology was formally dedicated. Named as first incumbent was Dr. Marion B. Sulzberger, director of dermatology, New York Skin and Cancer Unit, a division of the Bellevue Medical Center's University Hospital, and chairman, department of dermatology and syphilology of New York University Post-Graduate Medical School and the College of Medicine. The chair was made possible through the will of the late Dr. MacKee, who founded "the most complete, self-contained department of dermatology in the United States, encompassing in its own premises separate divisions of histopathology, mycology, surgery, allergy and immunology, pharmacy, physical therapy, hematology, photography, etc. This department, at the Skin and Cancer Unit of New York University–Bellevue Medical Center, has now trained well over a thousand postgraduate students coming from all over the world." Dr. MacKee, author of the textbook "X-Rays and Radium in the Treatment of Diseases of the Skin," was editor from 1909 to 1918, with the assistance of his wife Katherine, of the *Journal of Cutaneous and Venereal Diseases,* the predecessor of the present *A. M. A. Archives of Dermatology.*

NORTH CAROLINA

Personal.—Dr. Charles Capers Smith, who for two years has been studying neurology as a teaching fellow at the University of North Carolina School of Medicine, Chapel Hill, left recently for London, England, to spend a year in neurology at the National Hospital, Queens Square.——Dr. George D. Penick, assistant professor, department of pathology, University of North Carolina School of Medicine, Chapel Hill, received a travel award of $500 to attend the 20th International Physiological Congress in Brussels, Belgium, from the Federation of American Societies for Experimental Biology. The award was made on the basis of his paper, "Studies on Inactivation of Antihemophilic Factor in Clotting Plasma Systems," which he was to present at the congress.

OHIO

Society News.—New officers of the Academy of Medicine of Cleveland include Dr. A. Macon Leigh, president; Dr. Thomas D. Kinney, president-elect; and Dr. Chester R. Jablonoski, vice-president.

University News.—Dr. Azad A. Katchian, a graduate of the American University of Beirut, Lebanon, has been appointed personnel health physician at the Ohio State University Health Center, Columbus, to replace Dr. William W. Davis, who has accepted the position of medical director at North American Aviation. Dr. Davis will remain as assistant professor of preventive medicine and will help develop the graduate programs in aviation medicine and occupational medicine. Dr. Katchian has been affiliated with Edward Sanatorium in Naperville, Ill., and West Suburban Hospital, Oak Park, Ill.

Survey to Evaluate Hospital Care.—Under a grant from the U. S. Public Health Service, a three-year survey to develop a method for evaluating a hospital in terms of good patient care is being undertaken at Ohio State University Hospital, Columbus, under the direction of Daniel Howland, assistant professor of industrial engineering. The $180,000 project will measure the quality of patient care in every aspect of hospital operation. It is anticipated that, through evaluation of the effects of proposed changes in personnel and facilities on patient care, a significant reduction in the cost of hospital operations, in both dollars and manpower, may result.

OKLAHOMA

Ball Park Telephone.—The Tulsa Oilers have installed a telephone in the grandstand at the ball park for the exclusive use of physicians during the baseball season. A desk, pads, and pencils have also been provided.

Society News.—The Oklahoma State Radiological Association recently elected Dr. Lucien M. Pascucci, Tulsa, president; Dr. Simon Pollack, Tulsa, vice-president; and Dr. Sol Wilner, Tulsa, secretary-treasurer.

Founders Day Clinic at Tulsa.—The Tulsa County Medical Society will present its fourth annual Founders Day Clinic, Oct. 31-Nov. 1 at Tulsa. The clinic will open with a dinner meeting at the Mayo at 6:30 p. m. Wednesday. Dr. S. Buford Word, professor of obstetrics and gynecology, Medical College of Alabama, Birmingham, guest speaker of the evening, will discuss "Reconstruction of the Vagina." On Thursday at the Blue Cross-Blue Shield Building, 1215 S. Boulder St., a clinical pathological conference will be conducted by Dr. Otto Saphir, professor of pathology, University of Illinois College of Medicine, Chicago. Other speakers will be Dr. Walton R. Akenhead, associate professor of medicine, and Dr. Laurence H. Strug, clinical professor of surgery, both of Louisiana State University School of Medicine, New Orleans. There will be no charge except for meals. The clinic is jointly sponsored by the Tulsa County Medical Society, the Oklahoma division of the American Cancer Society, the Tulsa Academy of General Practice, the Tulsa County Heart Association, and the Arthritis and Rheumatism Foundation of Eastern Oklahoma.

OREGON

Personal.—Life memberships in the Oregon State Medical Society have been awarded to Drs. Augustus B. Dykman and Eugene P. Steinmetz, both of Portland. Dr. Dykman has been a member of the state society since 1922 and Dr. Steinmetz since 1920.

PENNSYLVANIA

Surgical Meeting in San Francisco.—The Hawthorne Surgical Society of the Graduate School of Medicine, University of Pennsylvania, Philadelphia, held its annual meeting on Wednesday evening, Oct. 10 in San Francisco during the convention of the American College of Surgeons.

Dr. Chapman Honored.—Dr. Leroy E. Chapman, Warren, was recently honored at Warren General Hospital when the Warren County Medical Society presented him with a plaque for 50 years of service as a doctor. Dr. Chapman who has served in the senate of the Pennsylvania General Assembly since 1930, was reelected last year for his eighth term. He is author of a study of problems of the aging in Pennsylvania and is a member of the Pennsylvania Cancer Commission, the Joint State Government Commission, and the Pennsylvania Historical and Museum Commission. He holds a plaque awarded by the Pennsylvania medical society for distinguished medical legislation.

Personal.—At the 109th annual commencement exercises of the Hahnemann Medical College and Hospital of Philadelphia, June 14, Dr. Donald Guthrie, surgeon-in-chief of the Guthrie Clinic of the Robert Packer Hospital in Sayre, was awarded the honorary degree of doctor of humane letters, and Mr. Francis Boyer, president of Smith, Kline & French Laboratories, Philadelphia, received an honorary doctorate of laws.

Philadelphia

Phi Delta Epsilon Lecture.—The Sigma chapter of the Phi Delta Epsilon Fraternity at Temple University School of Medicine will hold its ninth annual lectureship at 4 p. m., Oct. 31, in the auditorium of the medical school. The guest speaker, Dr. Charles R. Rein, associate professor of clinical dermatology and syphilology, New York University Post-Graduate Medical School, New York, will discuss "The Detection and Clinical Importance of Biologic False Positivity in Serologic Tests for Syphilis."

Dr. Kern Honored.—A testimonial dinner was recently given for Dr. Richard A. Kern, head, department of medicine, Temple University Medical Center, by the heads of departments and the medical staff. He was honored also at a testimonial dinner at the Philadelphia Cricket Club. It was given by former residents who were on his service at the Temple University Hospital, who presented him with a silver tray. Dr. Kern, who was recently named president-elect of the American College of Physicians, is a retired rear admiral in the Medical Corps, U. S. Navy, and has served as chief of medicine at Temple since 1946.

University News.—A grant of $166,466.39 from the Samuel S. Fels Fund has been awarded to the Fels Research Institute at the Temple University School of Medicine for the 1956-1957 fiscal year. The money will support studies in cancer research and gastroenterology under the direction of Dr. Harry Shay.——At their annual donor dinner, May 3, the Brith Sholom Women presented a check for $20,000 to Dr. Madison B. Brown, executive vice-president of the Hahnemann Medical College and Hospital of Philadelphia, representing the group's continued support of the Brith Sholom Laboratory for Cardiovascular and Pulmonary Research. The year's donation brings to $110,000 the total given to the facility since its dedication five years ago.——Dr. John H. Gibbon Jr., director of surgical research at Jefferson Medical College since 1946, has been advanced to head of the department of surgery and to the Samuel D. Gross Chair of Surgery. Dr. Gibbon, a former president of the American Surgical Association and consulting surgeon to Pennsylvania Hospital and Philadelphia Veteran's Administration Hospital, pioneered the development of the heart-lung machine used to take over functions of these organs during heart operations. He will occupy the positions held since 1950 by the late Dr. Thomas A. Shallow, who died last December.——At the graduation exercises of the Temple University School of Medicine June 14, the invocation was read by the Rev. Jan Frederick Mittemeyer, who came from Dutch Guiana to see his son, Bernhard, graduate in the class of 125 members. Drs. Thomas M. Durant and Bernard J. Ronis, both faculty and hospital staff members, presented their sons, John R. Durant and Max L. Ronis, with their diplomas. The elder Ronis is also a graduate of the school (class of 1934). Three other fathers, all graduates of the school—Drs. Alphonse V. Clement Sr., Brooklyn, N. Y. (class of 1935), Charles W. Delp Sr., St. Clair, Pa. (class of 1924), and Joseph C. Donnelly Sr., Philadelphia (class of 1924)—saw their sons graduate together.

Personal.—Dr. Catherine Macfarlane, professor of gynecology, Woman's Medical College of Pennsylvania, was honored as "Woman of the Year" by the Brith Sholom Women at their annual donor dinner, where a plaque was presented to her for outstanding service in the general field of public welfare and human relations.——Dr. Thomas E. McGraw has been appointed Philadelphia plant medical director of the Exide Industrial Division, the Electric Storage Battery Company, to succeed Dr. Gilbert B. Meyers, now with Radio Corporation of America. Dr.

McGraw is a staff member of Frankford Hospital.——Robert C. Baldridge, Ph.D., assistant professor of physiological chemistry, Temple University School of Medicine, has been named a consultant to the medical division of the Oak Ridge (Tenn.) Institute for Nuclear Studies. Dr. Baldridge will give counsel in studies relating to the effect of hormones on amino acid metabolism and protein synthesis, currently in progress at the institute. ——Dr. Carroll R. Mullen, former national president of the Alumni Association of Jefferson Medical College of Philadelphia, has been appointed professor and head of the department of ophthalmology at the college. He succeeds Dr. Arno E. Town, who will continue in the private practice of ophthalmology in New York. Dr. Mullen is attending surgeon and executive surgeon at the Wills Eye Hospital and serves as a consultant in ophthalmology at the Philadelphia General Hospital, Thomas M. Fitzgerald Mercy Hospital, Darby, and the J. Lewis Crozer Homeopathic Hospital, Chester.——On June 13 the city council adopted a resolution commending Dr. Isidor S. Ravdin, the only civilian surgeon called in as a member of the medical team that performed President Eisenhower's abdominal operation. The resolution reads, in part: ". . . . Dr. Ravdin, educated in a Philadelphia medical school and a surgeon in Philadelphia hospitals, has had an illustrious career spanning nearly 40 years. . . . Dr. Ravdin's tireless activity has made him a leader within the medical profession, and has contributed greatly towards Philadelphia's reputation as a major medical center. . . ."——Dr. Arthur F. Seifer, associate in orthopedics, Temple University Medical Center, delivered the presidential address at the May 4 meeting of the Philadelphia Orthopedic Club.——Dr. Ward D. O'Sullivan, formerly associate professor of clinical surgery at Cornell University Medical College, New York, and associate attending surgeon at New York Hospital, is director of surgery at Misericordia Hospital, where he conducts the surgical residency program.——Dr. John P. Turner, a former police surgeon and member of the board of education, was honored at the regular meeting of the Philadelphia County Medical Society, May 23, in recognition of the completion of 50 years in the practice of medicine. Dr. Turner was 22nd president of the National Medical Association in 1921 and its distinguished service medalist in 1946.——Dr. Thomas M. Durant of the Temple University Medical Center recently participated in the Ventnor Foundation meeting in Wiesbaden, Germany, in behalf of the German Intern-Exchange Programs, an arrangement by which exchangees spend 13 months in Germany and America as rotating interns. Dr. Durant spoke on "Management of Congestive Heart Failure." Those attending the conference were alumni of the program and medical educators who have been active in its operation. The effort is independent of any government agency but is conducted with the cooperation of the U. S. State Department.

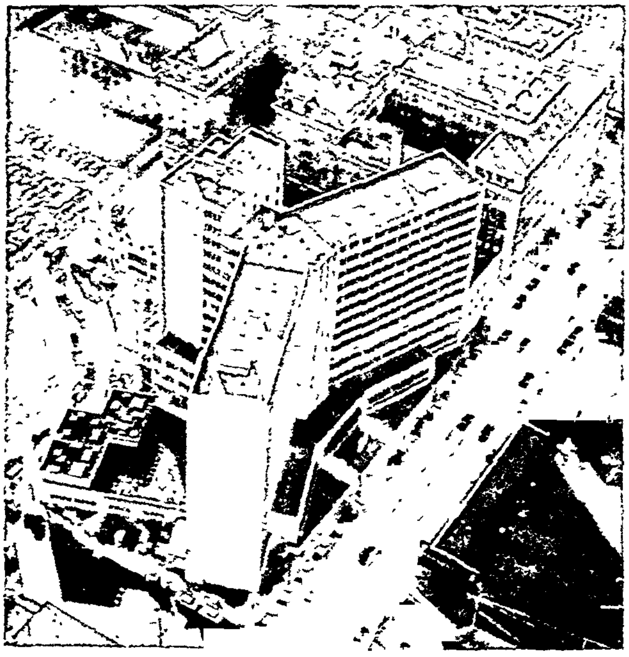
TENNESSEE

Society News.—Officers of the Tennessee Society of Pathologists include Dr. Frank C. Womack Jr., Nashville, president and councilor to the American Society of Clinical Pathologists; Dr. Chester K. Jones, Jackson, vice-president and president-elect; and Dr. George F. Bale, Memphis, reelected secretary-treasurer.

University News.—The University of Tennessee College of Medicine, Memphis, announces the following promotions: Drs. Garabed H. Aivazian, William J. Von Lackum, and Phineas J. Sparer, from assistant professor to associate professor in the department of psychiatry; Drs. William F. Murrah, department of ophthalmology, and Don L. Winfield, department of psychiatry, from instructor to assistant professor; Dr. Alvin J. Ingram, from assistant to assistant professor in the department of orthopedic surgery; and Drs. R. Beverly Ray and Moore Moore Jr., department of orthopedic surgery, and Drs. Henry J. Roberts and Margaret J. Halle, department of ophthalmology, from assistant to instructor.

Grants for Poliomyelitis Research.—The work of the Poliomyelitis Respiratory Center at Vanderbilt University Hospital, Nashville, will be supported during the coming year by a grant from the National Foundation for Infantile Paralysis of $54,724.74 that will be administered under the direction of Dr. O. Randolph Batson, associate professor of pediatrics. Research being conducted at the center includes studies of various breathing difficulties, the effects of prolonged bedrest, and complications associated with severe paralysis. An additional grant of $8,617 was made by the foundation for development of an iron lung that will adjust automatically to the patient's needs so that, through the muscle impulses he would normally use for breathing, he can control both the rate and depth of breathing with which the machine operates.

Baptist Memorial Addition.—The new Madison-East Building of Baptist Memorial Hospital, Memphis, erected and equipped at a cost of $8,250,000, adds nine patient floors and increases the capacity of the hospital to 800. The new building is so planned that it can be enlarged when necessary. According to Frank S. Groner, LL.D., administrator, a 25-year plan calls for 1,400 beds. The entire building is air-conditioned. Nine of the 13 floors are for hospital rooms, with a special penthouse for the radioisotope laboratory. The third floor has 19 operating rooms in which outlets for oxygen and anesthetics on two walls permit the surgeon to operate from either side of the room. Baptist Hospital has 1,500 employes, including 265 student nurses, 20 interns, and 21 residents. Its 400 doctors contributed more than $200,000 for the Madison-East Building.



Madison-East Building, forefront, flanked at right by original Baptist Memorial Hospital, in rear of which is nurses' dormitory.

Research Grants.—The University of Tennessee College of Medicine, Memphis, has been awarded a grant of $9,720 by the Institute of Arthritis and Metabolic Diseases of the U. S. Public Health Service to establish a special training program in the field of rheumatology. The program director for the project, which will be in the department of medicine of the City of Memphis Hospitals, is Dr. I. Frank Tullis, chief, division of medicine.——The National Heart Institute of the U. S. Public Health Service, the Atomic Energy Commission, and the Memphis Heart Association have awarded Nicholas R. DiLuzio, Ph.D., instructor in physiology, research grants totaling $28,712 for support of his studies on the harmful effects of exposure to radiation and his investigation of fat metabolism.——Dr. Edward H. Storer, assistant professor of surgery, has been given a $10,350 research grant by the National Cancer Institute of the U. S. Public Health Service for a project to produce stomach cancer in experimental animals and study the disease process. ——Dr. Robert C. Rendtorff, assistant professor of preventive medicine, has been awarded a $33,623 three-year research grant for the study of virus and parasite relationships by the National Institute of Allergy and Infectious Diseases of the U. S. Public Health Service.

TEXAS

Symposium on Carcinoma of the Breast.—The University of Texas M. D. Anderson Hospital and Tumor Institute, in conjunction with the University of Texas Postgraduate School of Medicine and the Texas division, American Cancer Society, will present a symposium on management of carcinoma of the breast in the Main Auditorium of the hospital, Houston, Nov. 9-10. The symposium will constitute a 10-hour course of formal teaching for American Academy of General Practice credit. The Friday morning program, 9 a. m., will consist of a review of "The Present Knowledge of the Spread of Cancer" by Dr. R. Lee Clark Jr., Houston; "Treatment Policies Based on Present Concepts" by Dr. Edgar C. White, Houston; and "Presentation of Cases Covering the Spectrum of Problems of Primary Treatment," with Drs. Clark, White, Gilbert H. Fletcher, Everett Lewis, and William O. Russell, Houston, serving on the panel. The afternoon meeting will be opened by Dr. Melvin A. Casberg, vice-president in charge of medical affairs, University of Texas, Austin, who will discuss "Surgical Treatment of Cancer of the Breast," which will be followed by presentation of "Present Concepts of Radiotherapy in Breast Cancer" by Dr. Fletcher. The afternoon program will be concluded by presentation of cases to illustrate problems of management of recurrences in local and regional areas. A get-acquainted hour, 5:30 p. m. at the Doctors' Club, will precede dinner at 7, when Dr. Ian G. Macdonald, associate clinical professor of surgery, University of California at Los Angeles School of Medicine, will speak on "Statistics in Breast Cancer." Dr. Macdonald will open the Saturday morning program with "Hormonal Management of Late and Disseminated Carcinoma of the Breast," which will be followed by presentation of cases.

WEST VIRGINIA

Politics.—The following physicians were elected at the May primary as members of county boards of education: Dr. E. Burl Randolph, Clarksburg, Harrison County (reelected); Dr. William P. Bradford, Moundsville, Marshall County (reelected); Dr. James W. Stokes, Hinton, Summers County (reelected); Dr. Richard F. Miller, Paden City, Wetzel County; and Dr. Paul L. McCuskey, Parkersburg, Wood County. Dr. Ward Wylie of Mullens was nominated on the Democratic ticket to succeed himself as a member of the West Virginia Senate from the Ninth Senatorial District, and Dr. Thomas G. Matney of Peterstown is the Democratic nominee to succeed himself as a member of the House of Delegates from Monroe County. Dr. James A. Rusmisell of Buckhannon was elected delegate from the Third District to the Republican National Convention, and Dr. Ward Wylie was named alternate delegate to the Democratic National Convention. Dr. William E. Neal of Huntington was nominated on the Republican ticket for representative in Congress from the Fourth Congressional District. Dr. Clinton W. Stallard of Montgomery received the nomination on the Democratic ticket for county commissioner in Fayette County, and Dr. John M. Cofer of Bergoo was nominated on the Democratic ticket for the same office in Webster County.

WISCONSIN

Society News.—The Wisconsin Society of Internal Medicine recently elected Dr. Karl H. Doege, Marshfield, president; Dr. Robin N. Allin, Madison, vice-president; and Dr. Paul G. LaBissoniere, Milwaukee, secretary-treasurer.

GENERAL

Course on Diagnostic Radiology.—The University of Wisconsin Medical School, Madison, will offer a postgraduate course (fee $20) entitled "Diagnostic Radiology," Nov. 6-8, under the direction of Dr. Lester W. Paul of the department of radiology. The course, designed especially for the general practitioner, is not confined to registrants in Wisconsin. Those interested may contact Dr. Robert C. Parkin, Assistant to the Dean, 418 N. Randall Ave., Madison, Wis.

Neurological Surgeons Meet in Chicago.—The sixth annual meeting of the Congress of Neurological Surgeons will take place at the Palmer House, Chicago, Nov. 1-3. The theme of the program is centered on the pituitary gland, its ophthalmologic, endocrine, and surgical aspects. Dr. Wilder G. Penfield, Montreal, Canada, the principal guest speaker, will discuss the function of the temporo-Sylvian fissure and will present a historical sketch, "Dawn of Medicine in the Aegean." Inquiries should be directed to the office of the Secretary-Treasurer, Dr. Philip D. Gordy, 1007 Delaware Ave., Wilmington, Del.

Cardiac Conference.—The fifth Western Cardiac Conference will be held at the Cosmopolitan Hotel, Denver, Nov. 5-10. The first three days will be devoted to sessions on clinical electrocardiography at the Veterans Administration Hospital. The last three days will be concerned with sessions on recent advances in cardiovascular disease, held at the Cosmopolitan Hotel. The sponsoring organizations are the Colorado Heart Association, the University of Colorado Medical Center, the Veterans Administration Hospital, the Fitzsimons Army Hospital, and the Colorado State Department of Public Health.

Tropical Medicine Society.—The American Society of Tropical Medicine and Hygiene will hold its fifth annual meeting at the Jung Hotel, New Orleans, Oct. 31–Nov. 3, under the presidency of Asa C. Chandler, Ph.D., Houston, Texas. The 21st annual Charles Franklin Craig Lecture, "The Role of Pharmacology in Determining the Rational Use of Therapeutic Agents," will be presented Wednesday at 2 p. m. by Leon H. Schmidt, Ph.D., Cincinnati. Norman R. Stoll, Sc.D., New York, will serve as moderator for a symposium on helminthic infections as the cause of disability and disease Thursday, 2 p. m. The dinner session will be held Friday at 7 p. m., when presentation of the Walter Reed medal will precede the presidential address, "The Interrelations of Nutrition and Infectious Diseases in the Tropics" by Dr. Chandler. In all, 87 papers are scheduled for presentation. Scientific exhibits will be on display.

Cancer Seminar.—The Southeastern States Cancer Seminar will be held at the George Washington Hotel in Jacksonville, Fla., Nov. 7-8 under the sponsorship of the Duval County Medical Society and the auspices of the Florida division of the American Cancer Society, the Florida State Board of Health, and the department of medicine of the Graduate School of the University of Florida. There will be no registration fee. The following panel discussions have been scheduled:

Management of Carcinoma of the Breast, Everett D. Sugarbaker, Jefferson City, Mo., Chairman.
Female Genital Neoplasm, Other Than Carcinoma of the Cervix, Willard M. Allen, St. Louis, Chairman.
Diagnosis and Treatment of Carcinoma of the Colon and Stomach, Michael R. Deddish, New York, Chairman.
Tumors of the Skin and Subcutaneous Tissue, George C. Andrews, and George T. Pack, New York.
Tumors of the Head and Neck, James E. Scarborough, Emory University, Ga., Chairman.

Society Election.—Newly elected officers of the Biological Photographic Association include Mr. H. Lou Gibson, Rochester, N. Y., president; Mr. Leo C. Massopust Sr., Milwaukee, vice-president; Miss Jane H. Waters, New York, secretary; and Mr. Albert Levin, Pittsburgh, treasurer.

Memorial Fund for Medical Research.—Between Nov. 4, 1955, and May 21, 1956, the Jane Coffin Childs Memorial Fund for Medical Research, 333 Cedar St., New Haven 11, Conn., appropriated $390,734 for support of cancer research projects and fellowships.

Atomic Scientists Available for Lectures.—The U. S. Atomic Energy Commission, the Oak Ridge National Laboratory, and the Oak Ridge Institute of Nuclear Studies announce that 102 scientists from Oak Ridge laboratories will be available to lecture, conduct seminars, and participate in colloquiums on request at universities throughout the country. A brochure listing the 102 speakers and the 165 different lecture subjects may be obtained by writing the Chairman, University Relations Division, Oak Ridge Institute of Nuclear Studies, P. O. Box 117, Oak Ridge, Tenn.

New Scientific Director of Multiple Sclerosis Society.—Dr. Thomas L. Willmon, for the past five years executive officer of the Navy's medical research laboratory at Bethesda, Md., has been appointed director of the medical and scientific department of the National Multiple Sclerosis Society, succeeding Frederick

L. Stone, Ph.D., who has assumed his duties in Washington as technical analyst and staff advisor for the U. S. Public Health Service extramural research and training programs. Dr. Willmon has conducted research in respiratory and cardiovascular physiology and has supervised basic medical research while serving in administrative posts in the Naval Medical Corps. In accepting the directorship, Dr. Willmon is leaving the naval service after 25 years, holding the rank of captain.

Kenny Foundation Scholarships.—The Sister Elizabeth Kenny Foundation announces a program of postdoctoral scholarships to promote work in the field of neuromuscular diseases, designed for scientists at or near the end of their fellowship training in either basic or clinical fields concerned with the problem of neuromuscular diseases. Kenny foundation scholars will be appointed annually. Each grant will provide a stipend for a five-year period at the rate of $5,000 to $7,000 a year depending upon the scholar's qualifications. Candidates from medical schools in the United States and Canada will be eligible. Information may be obtained from Dr. Edgar J. Huenekens, Medical Director, Sister Elizabeth Kenny Foundation, 2400 Foshay Tower, Minneapolis 2.

Educational Foundation.—The University Club (1 W. 54 St., New York 19) recently announced the formation of the Educational Foundation of the University Club, Inc. The purposes of the foundation include the receipt and administration of funds exclusively for scientific, literary, educational, and charitable purposes; the granting of scholarships, fellowships, or other forms of voluntary financial assistance to worthy students, teachers, and organizations duly established to carry on educational functions; the fostering, encouragement, and conduct of scientific, literary, or educational research; and the granting of funds for such research and study. The foundation will be operated on a nonprofit basis. Contributions (tax deductible) should be sent in care of Mr. Duncan R. Linsley, Educational Foundation of the University Club, Inc.

Grants to Medical Schools.—The Commonwealth Fund (1 E. 75th St., New York 21) announces unrestricted grants of $4,850,000 to seven university medical schools, bringing to a total of $12,600,000 the amount of such gifts to medical schools made by the fund since November, 1955. This is in addition to the sums expended for specific medical education projects during the fiscal year 1955-1956. Grants of one million dollars each were made to the Johns Hopkins University School of Medicine, Baltimore, and Stanford University School of Medicine, Stanford University–San Francisco; $750,000 to the University of Rochester (N. Y.) School of Medicine & Dentistry; $600.000 to Boston University School of Medicine; and $500.000 to each of the following: Albany (N. Y.) Medical College of Union University, George Washington University School of Medicine, Washington, D. C., and the University of Pennsylvania School of Medicine, Philadelphia.

Ford Foundation Grants to Medical Schools.—The Ford Foundation, New York, has announced grants totaling $21,750,000 to strengthen instruction in the 44 privately supported medical schools in the United States. The grants are in the amount of $500,000 to each of 43 four-year institutions and $250,000 to the two-year medical school at Dartmouth College, Hanover, N. H. They were authorized on the recommendations of a special advisory committee headed by Lee A. DuBridge, Ph.D., president of the California Institute of Technology, Pasadena. The foundation set up the advisory committee to develop plans for distributing 90 million dollars that the foundation appropriated last December to aid the instructional programs of the private medical schools. The grants are to be held by the recipient institutions as invested endowment for at least 10 years. During this time the income from the endowment may be expended for instructional purposes. Excluded from purposes of the grants are construction and research needs. After a 10-year period the medical schools will be free to use the principal sum as well as the endowment income.

CANADA

Gross Memorial Lecture.—The 19th annual Louis Gross Memorial Lecture, under the auspices of the Montreal Clinical Society, will be held in the Main Auditorium, Nurses' Residence, Jewish General Hospital, Montreal, Nov. 1, 8:30 p. m. Dr. Henry K. Beecher, Dorr Professor of Research Anaesthesia, Harvard Medical School, Boston, will discuss "New Work on Pain and Pain-Relieving Agents."

LATIN AMERICA

Seminar on Diarrheal Diseases.—The government of Chile will sponsor the first of a proposed series of intercountry seminars on prevention, diagnosis, and treatment of diarrheal diseases in childhood to be organized by the Pan-American Sanitary Bureau, Regional Office of the World Health Organization. The seminar, to be held in Santiago, Nov. 5-10, will bring together public health administrators, specialists in the field of maternal and child health, pediatricians, sanitary engineers, public health nurses, epidemiologists, bacteriologists, and others. It is scheduled to develop concrete proposals for program planning and specific techniques for diarrheal disease control.

CORRECTION

Aryl Sulfonylureas.—In the article by Drs. R. H. Unger and J. W. Davidson Jr. in The Journal Sept. 29, 1956, page 449, left-hand column, line 14, the word "tolbutamide" is in error. It should have been "carbutamide."

EXAMINATIONS AND LICENSURE

American Board of Anesthesiology: *Part I.* Various locations, July 19. Final date for filing application is Jan. 19. Sec., Dr. Curtiss B. Hickcox, 80 Seymour St., Hartford 15, Conn.

American Board of Internal Medicine: *Subspecialties. Cardiovascular Disease.* Chicago, Nov. 30. Final date for filing application was June 1. *Gastroenterology.* Philadelphia, April 5-6. Final date for filing application is March 1.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

American Board of Obstetrics and Gynecology: *Part I.* Various cities of the United States, Canada, and military centers outside the Continental United States, Feb. 1. Candidates must submit case reports to the office of the Secretary within thirty days of being notified of thei religibility to Part I. *Part II.* Chicago, May 16-25. Request for reexamination in Part II must be received prior to Feb. 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6, Ohio.

American Board of Ophthalmology: *Written.* Jan. 21. Final date for filing application was July 1. *Oral.* New York, May 23-27; Chicago, Oct. 7-11. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland 9, Maine.

American Board of Orthopaedic Surgery: *Oral. Part II.* Chicago, January 1957. Final date for filing application was Aug. 15. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

American Board of Pediatrics: *Oral. Part II.* San Francisco, Dec. 7-9. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

American Board of Physical Medicine and Rehabilitation: *Parts I and II.* New York City, June 8-9. Final date for filing application is March 1. Sec., Dr. Earl C. Elkins, 200 First St., S.W., Rochester, Minn.

American Board of Preventive Medicine: *Oral and Written. Public Health.* Philadelphia, Nov. 8-10. Sec., Dr. Ernest L. Stebbins, 615 N. Wolfe St., Baltimore, Md.

American Board of Psychiatry and Neurology: *Oral.* New York, Dec. 10-11 and New Orleans, Mar. 18-19. Final date for filing application is Sept. 10. Sec., Dr. David A. Boyd, Jr., 102-110 Second Ave., S.W., Rochester, Minn.

American Board of Radiology: Tampa, April 1-6. Final date for filing application is Jan. 1. Sec., Dr. B. R. Kirklin, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Part I.* Various centers throughout the United States and in certain military centers abroad, Oct. 31. *Part II.* New Haven, Nov. 19-20; Kansas City, Kan., Dec. 10-11; Los Angeles, Jan. 14-15; San Francisco, Jan. 17-18; Houston, Feb. 18-19; Nashville, Mar. 11-12; Boston, April 8-9, and New York, June 10-11.

American Board of Urology: *February 1957.* Sec., Dr. William Niles Wishard, 1711 N. Capital Ave., Indianapolis 7.

Board of Thoracic Surgery: *Written.* Various centers throughout the country, February 1957, and the closing date for registration is Dec. 1, 1956. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2.

GOVERNMENT SERVICES

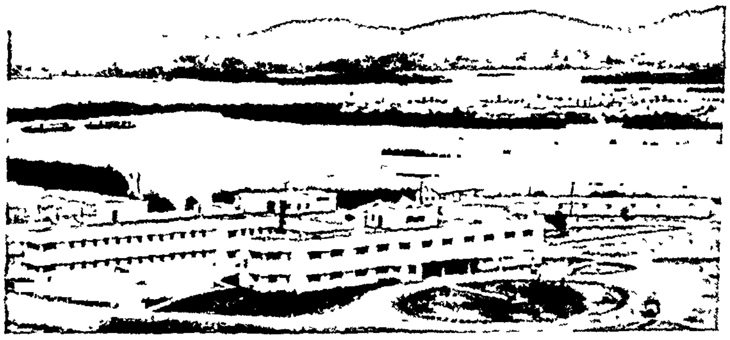
ARMY

Changes in Surgical Departments.—Lieut. Col. Curtis P. Artz, commander of the Surgical Research Unit at Brooke Army Medical Center, Fort Sam Houston, Texas, has left the military service to become professor of surgery at the University of Mississippi in Jackson. Colonel Artz entered the Army Medical Corps in 1948. He has been associated with the research unit at Brooke Army Medical Center for the last six years.

Col. Warner F. Bowers has arrived at the Tripler Army Hospital in Honolulu Hawaii, where he will be chief of the department of surgery, succeeding in that position Col. George Beatty, who has been assigned as chief of the department of surgery at the Valley Forge Army Hospital, Phoenixville, Pa.

NAVY

New Hospital at Guantanamo Bay.—At dedication ceremonies Sept. 18, 1956, Rear Adm. Bartholomew W. Hogan, surgeon general, accepted a new naval hospital for the medical department at Guantanamo Bay, Cuba. Having complete facilities for 100 bed patients and using the most modern construction materials, the new hospital will be air-conditioned throughout, the first naval hospital to be so equipped. At a cost of about $2,500,000, the new unit will replace the old wooden building used for many years. It will provide the latest medical facilities and care for naval personnel and their dependents stationed on the island. Capt. Lyle A. Newton, M.C., is the present commanding officer.



New naval hospital at Guantanamo Bay, Cuba (official U. S. Navy photograph).

Officials of various bureaus and offices of the Navy and the Department of Defense and representatives of the Army and Air Force participated in the dedication ceremonies. The hospital overlooks one of the most beautiful and best harbors in the world.

Reserve Officers Transfer to Regular Navy.—The following Naval Reserve medical officers have recently been commissioned in the Medical Corps of the regular Navy: Commander V. E. Seibert and lieutenants M. C. Shea Jr., J. F. Wurzel, H. O. Kretzschmar, J. A. Coulter, L. H. Seaton, Paul D. Mozley, A. A. McNitzky, H. R. Houston, L. N. Cahill, T. J. Grause, J. S. Garrison, and E. L. Bingham.

VETERANS ADMINISTRATION

New Advisory Committee Members.—Four new members have accepted appointments to the VA Special Medical Advisory Group as replacements for former members. The new members are Dr. Charles D. Shields, director, department of physical medicine and rehabilitation, Georgetown University, Washington, D. C., who replaces Dr. Donald A. Covalt, New York, whose membership has expired; Dr. Howard P. Rome, department of psychiatry, Mayo Clinic, Rochester, Minn., who replaces Dr. David A. Boyd Jr., department of psychiatry at the same clinic, whose five-year tenure has expired; Dr. Shields Warren of the Cancer Research Institute, Boston, who replaces Dr. Robert A. Moore, University of Pittsburgh, whose term has expired; and Mrs. Marion S. Bailey, associate director, National League for Nursing, New York City, who replaces Mrs. Elmira B. Wickenden, of Bronxville, N. Y., who has resigned.

This group meets quarterly to advise the administrator of veterans affairs and the chief medical director on the VA medical program.

PUBLIC HEALTH SERVICE

Advisory Committee Study to Help Hospitals.—A government advisory committee has been appointed to study and develop methods of adapting hospital facilities and services more closely to the varying needs of patients. Its objective is to help hospitals improve care and reduce costs, particularly for patients who need only limited services. Appointment of the committee was announced by Marion B. Folsom, Secretary of Health, Education, and Welfare.

The committee will review information on current practices and facilities and develop tentative recommendations for the design and organization of hospital units more closely related to the specific needs of patients, according to the severity of their illness or disability. The committee also will study ways in which hospital units can help provide effective services to some patients in their homes.

Dr. Russell Nelson, director, Johns Hopkins Hospital, Baltimore, will be the chairman. Other members of the advisory committee are Ray E. Brown, superintendent, University Clinics, University of Chicago, retiring president of the American Hospital Association; Robert Elman, M.D., department of surgery, School of Medicine, Washington University, St. Louis; Charles G. Roswell, hospital accountant, Montclair, N. J.; Ruth Sleeper, R.N., director, School of Nursing and Nursing Service, Massachusetts General Hospital, Boston; and Marion J. Wright, director, Jennings Memorial Hospital, Detroit.

Funds to Aid Teachers' Careers.—The Public Health Service's National Institute of Neurological Diseases and Blindness announces that funds are being made available to medical schools to strengthen existing clinical programs in advanced training in ophthalmologic and otologic diseases. The purpose is to stimulate the interest of more young physicians and scientists in careers as teachers and investigators in this field. Training grants also are available to basic science departments to expand postdoctoral training programs in the neurological sciences. Information may be obtained from the Chief, Extramural Programs, National Institute of Neurological Diseases and Blindness, National Institutes of Health, Bethesda 14, Md.

Research on Air Pollution.—Twelve grants for research on air pollution were announced Sept. 14 by Dr. Leroy E. Burney, surgeon general of the Public Health Service. The grants total $318,568. Six of the grants, totaling $177,548, are for new projects. The remaining six grants, amounting to $141,020, will continue support of projects already under way. These grants make a total of 32 that have been awarded since July, 1955, when air-pollution research was made a responsibility of the Public Health Service. All told, $780,137 has now been allocated to agencies, institutions, and individuals outside the federal government for such investigations.

DEATHS

Kimbrough, James Claude ⊕ Colonel, U. S. Army, retired, Silver Spring, Md.; born Nov. 5, 1887; Vanderbilt University School of Medicine, Nashville, Tenn., 1916; specialist certified by the American Board of Urology; member of the American Urological Association; fellow of the American College of Surgeons; entered the military service July 20, 1917; retired Aug. 31, 1948; since 1921 served almost exclusively as chief urologist at various Army hospitals; during World War II chief of the professional services division in the office of the chief surgeon of the European Theater of Operations; in 1945-1946, served as commanding officer of the Convalescent Hospital, Percy Jones Hospital Center, at Fort Custer, Mich.; awarded the Legion of Merit in 1945; later was chief of the urologic section, Walter Reed Army Hospital, Washington, D. C., and consultant in urology to the surgeon general, for liaison between the Army and the American Board of Urology; died Aug. 19, aged 68, of cancer of lung with metastasis.

O'Donnell, Alfred ⊕ Ellsworth, Kan.; born in 1873; University Medical College of Kansas City, Mo., 1900; member of the House of Delegates of the American Medical Association in 1925, 1926, and 1927; member of the founders' group of the American Board of Surgery; past-president of the Kansas Medical Society; fellow of the American College of Surgeons; member of the state board of health; for many years a member and for a time president of the school board; charter member and past-president of the Ellsworth Lions Club; for many years physician for the Union Pacific Railroad; served on the staff of the Ellsworth County Veterans Memorial Hospital, where he died June 26, aged 83, of pulmonary embolus and Parkinson's disease.

Rahman, Lincoln ⊕ Beverly Hills, Calif.; born in New York City Feb. 12, 1903; Cornell University Medical College, New York City, 1932; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychoanalytic Association and the American Psychiatric Association; assistant clinical professor of psychiatry at University of Southern California School of Medicine, Los Angeles; formerly associated with the U. S. Public Health Service Reserve; secretary of the Southern California branch, American Psychiatric Association, and vice-president of the Los Angeles Psychoanalytic Society; attending psychiatrist, Los Angeles County Hospital, Los Angeles; died Aug. 11, aged 52, of injuries received in an automobile accident.

Newburgh, Louis Harry, Valley Center, Calif.; born in Cincinnati in 1883; Harvard Medical School, Boston, 1908; professor emeritus of clinical investigation in internal medicine at the University of Michigan Medical School, Ann Arbor, where he joined the faculty in 1916; on the faculty of his alma mater from 1912 to 1916; specialist certified by the American Board of Internal Medicine; member of the American Society for Clinical Investigation; fellow of the American College of Physicians; the recipient of a certificate of merit for services in the Office of Strategic Research and Development during World War II; secretary of the special medical examining board during World War I; died July 17, aged 73.

Riter, Kersey Clyde ⊕ Salt Lake City; born in Logan, Utah, Dec. 8, 1906; Northwestern University Medical School, Chicago, 1937; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology, fellow of the American College of Surgeons; interned at the Passavant Memorial Hospital in Chicago; served a residency at the New York Post-Graduate Medical School and Hospital in New York City; veteran of World War II; served as a missionary in Switzerland; on the courtesy staffs of Dr. W. H. Groves Latter-Day Saints and St. Mark's hospitals; died July 23, aged 49.

Bardeleben, Walter, New York City; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1919; member of the Medical Society of the State of New York; died in the Memorial Center for Cancer and Allied Diseases June 27, aged 65, of carcinoma of the pancreas with metastases.

Becker, Charles Nicholas ⊕ Chicago; Chicago College of Medicine and Surgery, Chicago, 1913; served on the faculty of his alma mater; died in the Augustana Hospital Aug. 15, aged 72, of carcinoma of the pancreas.

Cinberg, Morris, New York City; University of the South Medical Department, Sewanee, Tenn., 1899; an associate member of the American Medical Association; died Aug. 10, aged 81, of cerebral vascular accident, arteriosclerosis, and congestive heart failure.

Easly, Philip Howard, Elyria, Ohio; St. Louis University School of Medicine, St. Louis, 1954; interned at the U. S. Naval Hospital in St. Albans, N. Y.; formerly a resident at St. John's Hospital in Cleveland; died July 20, aged 32.

Gardner, John Gould ⊕ Columbia, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1912; fellow of the American College of Surgeons; died Aug. 13, aged 76.

Graebner, Herbert ⊕ New York City; Milwaukee Medical College, Milwaukee, 1912; veteran of World War I; specialist certified by the American Board of Otolaryngology; member of the American Laryngological, Rhinological and Otological Society; formerly on the faculty of Cornell University Medical College; served on the staffs of the Manhattan Eye, Ear and Throat Hospital, New York Hospital, and the Willard Parker Hospital; died July 17, aged 66, of carcinoma of the stomach.

Gram, Gunnar, Geneva, Wis.; Chicago Medical School, Chicago, 1927; veteran of the Spanish-American War; died April 26, aged 76, of congestive heart disease and arteriosclerosis.

Hallowell, Albert V., Commander, U. S. Navy, Ocala, Fla.; born in Philadelphia Jan. 5, 1901; Hahnemann Medical College and Hospital of Philadelphia, 1924; veteran of World War II; active duty in the regular U. S. Navy began July 21, 1950; attached to the U. S. Navy Bureau of Medicine in Washington, D. C.; served as associate professor of otorhinology at his alma mater; formerly on the staff of the Hahnemann Hospital in Philadelphia; died in the U. S. Naval Hospital, Bethesda, Md., July 27, aged 55, of carcinoma of the bladder.

Hambly, Scott B., Morrice, Mich,; Michigan College of Medicine and Surgery, Detroit, 1897; died June 29, aged 84, of carcinoma of the bladder and prostate.

Holyfield, H. N. ⊕ Brandon, Miss.; Gate City Medical College, Texarkana, Texas, 1906; died July 26, aged 77.

Jackson, Jeremiah, Evansville, Ind.; Medical College of Indiana, Indianapolis, 1897; died in St. Mary's Hospital April 26, aged 86, of fractured pelvis as the result of a fall and coronary insufficiency.

Jackson, Norborn Herbert, Dardanelle, Ark.; Arkansas Industrial University Medical Department, Little Rock, 1901; died July 10, aged 80.

Johnson, Hal Glenn, Dundee, Miss.; Vanderbilt University School of Medicine, Nashville, Tenn., 1911; past-president of the Tunica County Medical Association; died Aug. 17, aged 68.

Jones, Dudley Watson ⊕ Jackson, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1900; past president and formerly member of the council of the Mississippi State Medical Association; served as a member of the council of the Southern Medical Association; died July 27, aged 86.

⊕ Indicates Member of the American Medical Association.

King, Aubin Tilden ⊕ Major, U. S. Army, *retired, San Jose, Calif.*; University of Virginia Department of Medicine, Charlottesville, 1911; member of the American Psychiatric *Association; veteran* of World War I; entered the Medical Corps *of the U. S. Army* in 1920; retired Sept. 30, 1936, for disability in line of duty; died in the Letterman Army Hospital, San Francisco, July 11, aged 80, of thrombosis of the right middle cerebral artery, subdiaphragmatic abscess, cholecystitis, and bleeding duodenal ulcers.

Koerber, Kenneth Armin, *Philadelphia*; University of Pennsylvania School of Medicine, Philadelphia, 1930; member of the Medical Society of the State *of Pennsylvania; certified by the National Board of Medical Examiners; at one time medical director* of the Cramp Shipbuilding *Company; served on the staff of the* Germantown Dispensary and Hospital; *died in the Philadelphia* General Hospital July 24, aged 50, of agranulocytosis.

Krieger, George Madison ⊕ Michigan City, Ind.; Miami Medical College, Cincinnati, 1906; member of the American Academy of Ophthalmology and Otolaryngology; died in St. Anthony Hospital May 22, aged 74, of coronary sclerosis.

Langstadt, Arthur ⊕ Flushing, N. Y.; Ludwig-Maximilians-Universität Medizinische Fakultät, München, Bavaria, Germany, 1909; died in the New York City Hospital, New York City, July 20, aged 72, of myocardial infarction.

McClanahan, Zenas H. ⊕ Colorado Springs, Colo.; Colorado School of Medicine, Boulder, 1894; fellow of the American College of *Surgeons; past-president of the El Paso County Medical Society; on the staffs of the* Memorial Hospital, St. Francis Hospital, *and the* Glockner-Penrose Hospital, *where he died July 6, aged 85, of cerebral thrombosis.*

McGrew, John Merritt ⊕ Wellington, Kan.; University of Kansas School of Medicine, Kansas City, 1927; veteran of World War I; on the staff of St. Luke's Hospital; died in St. Francis Hospital, Wichita, July 25, aged 56, of chronic nephritis and uremia.

MacLean, Aubrey Bertram, New York City; McGill University Faculty of Medicine, Montreal, Quebec, Canada, 1919; died Aug. 1, aged 60, of carcinoma of the stomach.

Magaziner, William Edward, *Philadelphia*; Medico-Chirurgical College of Philadelphia, 1903; *an associate member of the American Medical Association; on the staffs of the* St. Luke's Hospital *and the* Lankenau Hospital, *where he died July 13, aged 73, of heart disease after an operation.*

Moffatt, Benjamin Harrison ⊕ Shelby, Ohio; Medical College of Virginia, Richmond, 1915; for many years city health commissioner; on the staff of the Shelby Hospital, where he died July 28, aged 67, of coronary occlusion.

Mogavero, Francesco ⊕ Philadelphia; born in Philadelphia Sept. 28, 1902; University of Pennsylvania School of Medicine, Philadelphia, 1925; certified by the National Board of Medical Examiners; specialist certified by the American Board of Surgery; member of the American Trudeau Society; fellow of the American College of Surgeons and the International College of Surgeons; on the staffs of the Doctors Hospital and the Misericordia Hospital, where he died July 22, aged 53, of cerebral hemorrhage.

Mostkowitz, Israel, Jamaica, N. Y.; Long Island College Hospital, Brooklyn, 1910; member of the Medical Society of the State of New York and the American College of Gastroenterology; on the staff of the Queens General Hospital; died July 31, aged 60, of subacute myelogenous leukemia.

Moyer, John Sanford, Metuchen, N. J.; University of Pittsburgh School of Medicine, Pittsburgh, 1921; certified by the National Board of Medical Examiners; specialist certified by the American Board of Otolaryngology; member of the Medical Society of the State of New York and the American Broncho-Esophagological Association; fellow of the American College of Surgeons; veteran of World War I; served on the staff of the Manhattan Eye, Ear and Throat Hospital in New York City; died in the Muhlenberg Hospital, Plainfield, July 10, aged 60.

Nagle, William Thomas, Southington, Conn.; Medico-Chirurgical College of Philadelphia, 1914; member of the Connecticut State Medical Society; veteran of World War I; on the staff of the Bradley Memorial Hospital; died July 17, aged 64, of carcinoma of the lower jaw.

Neesen, Victor, *Fort Lauderdale, Fla.*; Long Island College Hospital, Brooklyn, N. Y., 1894; *died June 10, aged 83, of arteriosclerotic heart disease.*

Nuckols, Ernest Benjamin ⊕ Cumberland, Va.; Medical College of Virginia, Richmond, 1908; a member of the staff of the Southside Community Hospital in Farmville; died July 11, aged 78, of cancer.

Olivier, Charles Kossuth, Lafayette, La.; Medical Department *of Tulane University* of Louisiana, New Orleans, 1910; an associate *member of the American Medical Association; served as director of the parish board of health; died July 10, aged 75, of coronary thrombosis.*

Pacelli, Joseph Francis ⊕ New York City; Hahnemann Medical College and Hospital of Philadelphia, 1932; died in the University Hospital July 7, aged 51, of ulcerative gangrene of the leg and mouth.

Peterson, Frank Joseph, New York City; Fordham University School of Medicine, New York City, 1919; member of the Medical Society of the State of New York; on the staffs of the Bronx Eye and Ear Infirmary and St. Elizabeth's Hospital; died Aug. 3, aged 60, of carcinoma of the right kidney.

Porter, John Thomas ⊕ Baytown, Texas; Chicago Medical School, Chicago, 1935; interned at the Illinois Central Hospital in Paducah, Ky.; served a residency at St. Louis Southwestern Hospital in Texarkana, Ark.; veteran of World War II; died in the Hermann Hospital, Houston, June 28, aged 48, of cirrhosis of the liver and diabetes mellitus.

Poust, George Alvin, *Hughesville, Pa.; Jefferson Medical College of Philadelphia, 1895; an associate member of the American Medical Association; veteran of World War I; associated with the Muncy Valley (Pa.) Hospital; died July 12, aged 87.*

Proctor, Feaster Le Grand, Forrest City, Ark.; University of Nashville (Tenn.) Medical Department, 1898; served in France during World War I; died in the Veterans Administration Hospital, Memphis, Tenn., July 11, aged 80, of myocardial infarction.

Pulese, Felix L., Southold, N. Y.; New York Homeopathic Medical College and Flower Hospital, New York City, 1928; member of the Medical Society of the State of New York; was with the U. S. Public Health Service and served as a lieutenant commander in the Coast Guard during World War II; attending physician at the Eastern Long Island Hospital in Greenport; on the staff of the Veterans Administration Hospital in Northport, N. Y., where he died July 18, aged 51, of arteriosclerotic heart disease.

Reid, Stewart Woods, West Hartford, Conn.; Yale University School of Medicine, New Haven, 1913; formerly member of the board of education of Hartford; died July 24, aged 70, of carcinoma of the lung.

Reynolds, Harry St. Clair ⊕ *Norwich, Conn.*; Yale University School of Medicine, New Haven, 1910; at one time on the faculty of his alma mater; served on the staffs of the Hartford (Conn.) Hospital and the Grace-New Haven (Conn.) Community Hospital; at one time on the staffs of the Institute of Living in Hartford and the Connecticut State Prison; died July 19, aged 75, of acute dilatation of the heart.

Richeson, Hugh Harding, Louisville, Ky.; University of Louisville School of Medicine, Louisville, 1914; an associate member of the American Medical Association; veteran of World War I; served on the staffs of Childrens Hospital and the Kentucky Baptist Hospital, where he died July 24, aged 69, of adenocarcinoma of the rectum.

FOREIGN LETTERS

FINLAND

Status of Immunization.—In *Nordisk medicin* for July 19, Dr. B. Landtman points out that in 1954 a law was enacted rendering BCG vaccination compulsory under certain conditions. For example it is compulsory for 19-year-old tuberculin-negative persons. At present 80% of Finnish children have had this vaccination and, of the 181 children admitted in recent years for tuberculous meningitis to the Children's Hospital in Helsinki, only 2 had been properly vaccinated with BCG vaccine. Virtually all children are vaccinated against whooping cough and diphtheria either at child welfare centers or privately, usually between the ages of 3 and 9 months, revaccination being undertaken when school age is reached. Tetanus is rare in Finland, and systematic vaccination against it has not been attempted.

Pyloric Stenosis.—Dr. A. Backman in the same issue reports a series of 34 patients with hypertrophic pyloric stenosis, of whom 28 were boys. The diagnosis in most cases was verified by roentgenograms. There were, however, four patients in whom the radiological findings were not quite typical but in whom the clinical evidence was strong enough in itself to warrant the diagnosis. Medical treatment was given to 21 patients (with one death) and 13 were operated on (with four deaths). The medical treatment consisted of giving 1 or 2 drops of methylscopolamine nitrate by mouth six to eight times daily. The surgical treatment consisted of the Fredet-Ramstedt operation. Medical treatment should be tried first, although it takes more time. The success of the surgical treatment depends to a large extent on skilled preoperative and postoperative treatment.

FRANCE

Electroencephalographic Findings in Paroxysmal Tachycardia.—R. Gerard and co-workers at the meeting on May 13 of the French Society of Cardiology stated that (1) in 13 of 25 patients with paroxysmal tachycardia the tracings between the paroxysms were normal; (2) in the other 12 the only evidence of abnormality was a definite but variable degree of hyperexcitability; and (3) some patients complained of pain in one or both temporal regions and had a lowered convulsive zone. No specific electroencephalographic evidence of epilepsy was found in these patients. Antispasmodics were given to those patients who were hyperexcitable or who had a lowered convulsive zone.

Levarterenol.—At the same meeting R. Legrand and co-workers showed that levarterenol induces bradycardia, anomalies of P waves, variations of the P-Q interval, and extrasystoles capable of causing supraventricular or ventricular tachycardia in healthy as well as diseased subjects. Levarterenol may induce coronary occlusion, even in patients who are in good health. The drug should, therefore, be given with caution. Its use is not recommended in the treatment of paroxysmal tachycardia, and it is contraindicated in patients with ventricular tachycardia or auriculoventricular dissociation.

Hydroelectrolytic Metabolism and Postoperative Reequilibration.—E. Delannoy and co-workers say that those patients who suffer significant losses or protracted loss of weight after operation raise difficult problems of maintenance of the hydroelectrolytic and nitrogen balance (*La semaine des hôpitaux de Paris,* volume 32, 1956). Neither clinically nor by measuring the electrolytes in the plasma is it possible to decide on the amount of therapeutic agents required. In complex cases an evaluation of the intake and output of fluids and of sodium, potassium, and nitrogen is essential. If no abnormal losses are observed, dextrose infusions should be given for the first three days and 50 mEq. of potassium chloride daily. Only after four or five days is saline solution necessary. In the event of abnormal losses, these should be exactly made up, but the urinary output of sodium may be disregarded in the first few days. If there is protracted loss of weight, a positive nitrogen balance must be established.

Radiographic Study of Poliomyelitis of the Spine.—A. Grossiord and co-workers (*La semaine des hôpitaux de Paris,* volume 32, 1956) state that, in patients with poliomyelitis of the spine, before scoliosis is reported, films should be taken in corrected decubitus position, especially in frontal projection on the spine placed in forced lateral flexion. Only such a technique, supplementing the clinical data, allows a measurement of the deformity, a valid comparison between the successive films, and a reliable prognosis.

Hypertension Due to Pheochromocytoma.—Laroche and Reboul (*La semaine des hôpitaux de Paris,* volume 32, 1956) say that pheochromocytoma may cause permanent hypertension without paroxysmal signs. The condition is generally serious, developing rapidly and accompanied by symptoms associated with hyperadrenalemia. Biological tests for hyperadrenalemia are not reliable. In doubtful cases one should attempt to detect the adrenal tumor by means of roentgenograms, including retropneumoperitoneum. Treatment of pheochromocytoma is surgical. Its prognosis has been improved by the use of levarterenol, but the ultimate prognosis should always be reserved, because hypertension may recur within a few months of the removal of the tumor.

Malignant Hypertension.—P. Milliez and co-workers (*La semaine des hôpitaux de Paris,* volume 32, 1956) say that the role of a disturbance in unilateral renal arterial circulation in initiating certain arterial hypertensions is indisputable. The possible ineffectiveness of nephrectomy is merely evidence that the angiopathy had escaped its preliminary cause when this became detectable. The presence of unilateral lumbar pains and hematuria in a hypertensive subject should encourage further careful examination. Nephrectomy, in the case of unilateral renal lesions, whatever their cause, should be performed. It may, however, in some ill-defined manner, cause circulatory disturbances in the healthy kidney, which results in an aggravation of the hypertension and renal insufficiency.

Hypertension Treated with Rauwolfia.—Senechal and co-workers (*La semaine des hôpitaux de Paris,* volume 32, 1956) observed a young woman who was treated from 1946 to the time of writing for severe arterial hypertension. Her blood pressure had risen to 250/190 mm. Hg, and the treatment used had proved ineffective. She had become pregnant twice, but both pregnancies ended in miscarriage. Starting in October, 1954, she was given Rauwolfia, and her blood pressure returned to almost normal values (140/100 mm. Hg). She again became pregnant and was delivered of a normal infant.

INDIA

Amebiasis.—Kasliwal and Bhatia (*Journal of the Indian Medical Association,* Aug. 16, 1956) report the results of needle biopsy of the liver in patients with chronic intestinal amebiasis. The patients were examined for evidence of any associated infection such as malaria that might affect the liver. Thirty patients with only amebic lesions were selected for liver biopsy. The main findings in their order of frequency were lymphoma, diffuse parenchymal liver cell damage, disorganization of hepatic cell plates, focal necrosis, and portal infiltration. These were consistent with the diagnosis of subacute hepatitis. The changes are caused by Endameba histolytica, not by the bacterial associates, and are probably reversible.

The items in these letters are contributed by regular correspondents in the various foreign countries.

Railway Accident Relief Car.—Medical relief for victims of accidents on Central Railway's broad-gauge line is now provided for by an accident relief car, a miniature hospital on wheels. Designed by the mechanical and medical departments of the Central Railway, the car is the first of its kind in India. It has an operating room and ward accommodations for 18 patients. The operating room equipment embodies the latest devices, used in battleships, to withstand vibration while the train is in motion. It has its own sterilizing equipment, a kitchen, hot and cold running water, and a refrigerator. Members of the railway's St. John Ambulance Brigade will accompany the car, in addition to the normal complement of medical and nursing staff. These members are all potential blood donors.

Tuberculosis Services.—To train a sufficient number of persons for tuberculosis services, the government proposes to subsidize the establishment of about 15 tuberculosis demonstration and training centers under the second Five Year plan. These centers will train tuberculosis workers of all categories and also demonstrate the latest techniques in the diagnosis and prevention of the disease. Three such centers at New Delhi, Trivandrum, and Patna were established under the first plan. Two more are being established at Madras and Nagpur with the assistance of the World Health Organization. The centers to be established under the second plan will consist of (1) an epidemiological section for mass x-ray screening and BCG vaccination, (2) a clinical section for diagnosis and treatment, (3) a bacteriological section, and (4) a domiciliary service under the direction of a public health nurse. A full-time director will supervise the working of all four sections and will be responsible for coordinating their work from the preventive viewpoint.

Typing Poliomyelitis Virus.—In an article in the *Indian Journal of Medical Sciences* (10:511 [July] 1956), C. S. Swaminathan has recorded the antigenic typing, by means of tissue cultures, of strains of poliomyelitis virus isolated in Bombay. The viruses were isolated from the stools of patients with clinical cases of poliomyelitis and their contacts by inoculation of rhesus monkeys. Throughout the investigation the hyperimmune antiserums against poliomyelitis virus types 1, 2, and 3 supplied by the United States National Foundation for Infantile Paralysis were used. Of the 57 strains, 54 belonged to type 1, 2 to type 2, and 1 to type 3. Of the two type-2 strains, one was isolated from a contact of a patient during a period between epidemics and the other from a patient during the epidemic period.

SWITZERLAND

Carcinogens in Foods.—R. Truhaut (*Oncologia* 9:84, 1956) states that, in view of the carcinogenic action of dulcin, a synthetic sweetener, a foreign substance, in order to be approved as a food additive, should be shown through prolonged experimentation to be devoid of harmful effects in general and in particular of carcinogenic effects. Standards of purity for foreign substances to be added to foods are most important, because the harmful effects of additives are often attributable to impurities. This is especially true of dyes.

Consumption of Cigarettes by Physicians.—O. Gsell sent a questionnaire concerning their smoking habits to physicians and received 4,105 responses (*Schweiz. med. Wchnschr.* 86:675, 1956). Sixty-one per cent of the physicians (23% of the female physicians) were habitual smokers; 38.5% (9% of the women) smoked more than 20 cigarettes per day; 60% of the male smokers and 99% of the female smokers smoked only cigarettes; 47% of the smokers inhaled; and 48% of the male smokers used filters. There was no difference in smoking habits of physicians living in cities and those living in the country.

Influence of Amphetamine on Hydroxycorticosteroids.—Recognizing that the injection of epinephrine appears to stimulate the secretory activity of the adrenal cortex, Muller and co-workers (*Schweiz. med. Wchnschr.* 86:688, 1956) studied the variations in serum 17-hydroxycorticosteroids under the influence of dextroamphetamine. Although devoid of the peripheral sympatheticomimetic action of the levoisomer, this derivative possesses, like epinephrine, properties stimulating to the central nervous system. In the eight hours that followed the taking of dextroamphetamine in relatively strong doses (15 to 25 mg.), there was an increase in the serum level of the 17-hydroxycorticosteroids. The existence of a spontaneous nyctohemeral variation of the 17-hydroxycorticosteroids of the blood indicates a relation to the hours of the day when the experiments were conducted. After the taking of amphetamine, the average elevations of the 17-hydroxycorticosteroids, in relation to the control values measured at the end of the morning, the afternoon, and in the evening, were 48, 41, and 92% respectively.

After the taking of amphetamine, the leukocytes and the eosinophils behaved in general as after the administration of corticotropin and cortisone, but there was no correlation between the degree of elevation of the steroid level and the variation of the differential leukocyte count. The mechanism by which amphetamine raises the steroid level is difficult to determine. The authors believe that the elevation of the steroid level observed after the administration of amphetamine, as well as the signs of adrenal hyperfunction noted in animals under the influence of epinephrine, is based on the suprahypophyseal action common to these two substances. The central action of the epinephrine, if it seems analogous to that of the amphetamine, is, however, less intense and much more fleeting. This could explain why the infusion of epinephrine has not raised the steroid level in man.

Limits of the Treponemal Immobilization Test.—The serologic reactions to lipid antigens being insufficient, numerous laboratories now use the treponemal immobilization test. J. Delacretaz (*Schweiz. med. Wchnschr.* 86:645, 1956) states that in syphilitic patients the treponemal immobilization test becomes positive at the end of the primary period or at the beginning of the secondary period (later than the classic serologic reactions). In the absence of treatment, it remains positive during the entire development of the disease without showing the same tendency as the classic reactions to spontaneous return to negative. In such treponematoses as yaws, bejel, and pinta, the treponemal immobilization test may be positive. In healthy subjects and in patients with nontreponemal diseases, the treponemal immobilization test is always negative. This is particularly important in checking biologically false reactions of the classic serologic tests. Like the classic serologic reactions, the treponemal immobilization test is more likely to become negative under the influence of the treatment according to how early in the disease the treatment is undertaken. As a general rule, the treponemal immobilization test becomes negative later than the classic serologic reactions under the influence of treatment, but this rule has certain exceptions. There is no assurance that the persistence of the immobilizing antibodies in the serum of a properly treated patient is incompatible with cure. A treponemal immobilization test remaining positive thus is not by itself an indication for continuing treatment. The author has not observed reversion to positive after the treponemal immobilization test has become negative. A negative treponemal immobilization test (repeated after three months in order to exclude all possibility of technical error) is thus presumptive evidence of cure. The author found the test to be indicated chiefly when positive classic serologic reactions were not accompanied by any sign of syphilis or when lesions suspected of being due to late syphilis were accompanied by negative classic serologic reactions.

Osmotic Nephroses.—Morard (*Helvet. med. acta* 23:215, 1956) reported a series of seven patients with nephropathies similar to the so-called osmotic nephrosis. These patients were given dextrose solution intravenously in amounts not exceeding the therapeutic norms or the tolerance to saccharides, but the preexistence of hyponatremia and the severe liver dysfunction seem to have potentiated, in each of these patients, the morphological expression of the osmotic imbalance. The author investigated the effects of giving dextrose solution in rabbits with electrolytic imbalance or hepatic insufficiency. One group of animals received a dextrose overloading of 15 gm. per kilogram of body weight intravenously; a second group received an overloading of 15 gm. per kilogram, together with a saline depletion by means of peritoneal dialysis, taking care not to modify the weight of the animals; and a third group received a purely hydric overloading aggravated by a loss of salt through peritoneal dialysis. Comparison of the histological changes indicated osmotic hepatonephrosis and that the saline depletion reinforced the osmotic action of the dextrose. Several factors may produce this morphological constancy, provided they disturb the electrolyte balance between the cell and its medium. An additional study was carried out in which the hepatotoxic effect of cinchophen was associated with dextrose overloading of 15 gm. per kilogram of body weight. The author found that the nephron reaction to the dextrose injection was not reinforced by the liver damage produced by cinchophen, but, for several reasons, this unsuccessful attempt does not negate the role of hepatic dysfunction in potentiating the osmotic nephrosis.

Ion Exchange.—By giving a salt-poor diet with the addition of sodium bicarbonate, P. Jeanneret (*Helvet. med. acta* 23:60, 1956) studied mineralocorticoid activity under conditions of normal sodium and low chloride intake and excretion. Under these circumstances, desoxycorticosterone acetate produces a marked retention of sodium and a significant loss of potassium, with no water retention. These observations, correlated with other studies where chloride was given without sodium, show that mineralocorticoid activity primarily affects tubular sodium reabsorption and that chloride retention is only a consequence of sodium retention. The potassium loss is interrelated with sodium retention, while the retention of chloride plays no part in this process. Water retention incidental to mineralocorticoid activity is not dependent solely on sodium retention; chloride also must be retained. Sodium retention alone does not lead to water retention. This last observation shows the need for reevaluation of the prevailing concept of the role attributed solely to sodium in water retention and points back to the classic view, that both sodium and chloride (salt) retention are necessary for formation of edema. With regard to dietetics, these results show that a sodium-poor diet prevents all direct steroid effects on electrolyte metabolism. This protecting effect, which is highly desirable when patients with normal adrenal cortex are treated with steroids having mineralocorticoid activity (cortisone, hydrocortisone, and fludrocortisone), is neutralized by sodium chloride and by other sodium salts. With sodium bicarbonate the potassium loss is much more pronounced than with sodium chloride. Alkalinizing sodium salts are therefore strictly contraindicated in these circumstances. When, on the other hand, a chloride such as ammonium chloride is given alone, the situation remains the same as with a salt-poor diet and no mineralocorticoid activity can be elicited.

Placental Extracts.—S. Rauch (*Helvet. med. acta* 23:75, 1956) in a study of human placental extracts concluded that the placenta is rich in enzymes, hormones, and mucopolysaccharides. These substances, however, are not contained in all the extracts. Their presence depends on the manner in which the extracts are prepared. The author considered four commercial preparations, three of which (extracts B, C, and D) were extracted according to Filatov's method, whereas the fourth extract (extract A) was prepared by the cold method. On the average, the most successful clinical results are obtained with extract A. The author made chemical and biological tests on these extracts in an attempt to find histochemical relations. In extract A, he found the following characteristics not found in the other extracts: (1) a high alkaline and acid phosphatase content; (2) an albumin fraction with amino acids, which can be electrophoretically demonstrated; (3) a high content of mucopolysaccharides and substances that migrate electrophoretically with beta-globulins; and (4) the strongest respiratory stimulating effect with a low-concentration optimum, i. e., with a 5% solution of the extract. This can be partly accounted for in terms of the ferment and hormone content, which, in the case of the other extracts, is lost as a result of the heating of the preparations. The component that stimulates breathing need not be identical with that which stimulates proliferation. Microimplantations, obtained by the same conservative method, were much less effective than the extract. The factors that exert the most stimulating effect on the tissues still remain unknown. They do not appear to form a part of the protein fraction, but rather of the water-soluble substrate. The stimulating effect on the breathing is largely confined to the mesenchymatous tissue; the epithelial tissue barely reacts at all. In view of these findings on the placental extracts, it is impossible as yet to give exact indications for their therapeutic use. The most favorable results are to be expected in the case of processes of the mesenchymatous tissues and, in that field, mainly on the strength of their influence on the intracellular ground substance.

UNITED KINGDOM

Tranquilizing Agents.—The Council of the Pharmaceutical Society of Great Britain is concerned about the situation produced by the recent introduction of a number of new products commonly known as "tranquilizers." Although they are not advertised to the public, a widespread public knowledge of them has been created by newspaper articles, and there is a substantial demand for them otherwise than on prescription. The indiscriminate use of such drugs is against the public interest, and pharmacists are urged not to display them or to supply them unless satisfied they will be taken on medical advice.

Mental Illness in Scotland.—Voluntary patients now represent practically 72% of the total admissions to mental hospitals in Scotland, according to the 1955 annual report of the General Board of Control for Scotland. Although, compared with the previous year, there was an increase of 657 in the number of admissions, these were exceeded by discharges and deaths, so that at the end of the year there were 57 fewer patients in mental hospitals than in 1954. All but one of the mental hospitals in Scotland were built more than 50 years ago. Television is often successful in stimulating the interest of chronic and apathetic patients. Several hospitals now supply attractive evening or party dresses for women patients to wear on special occasions such as dances, and two conveniently placed hospitals have arranged for parties of patients from one hospital to visit the other, alternating each month. These visits, during which football and billiard matches and other forms of entertainment are arranged, are greatly appreciated by the patients of both hospitals.

Two Americans Honored.—The Royal College of Surgeons has conferred the honorary fellowship of the college on Dr. I. S. Ravdin, of the University of Pennsylvania, who will visit London in December to deliver the Moynihan Lecture before the college. The Council of the Royal Institute of Public Health and Hygiene has appointed Prof. Philip Drinker, of Harvard University, as the Harben Lecturer for 1956. The subject of Professor Drinker's lectures, which will be delivered in May, 1957, is "Air Pollution and the Public Health."

Generalized Vaccinia.—Four cases of generalized vaccinia in one family were reported by a health officer in the East End of London. Two weeks after the youngest member of the family, aged one year, had been vaccinated, the 6-year-old sister was admitted to the hospital with a fever and rash of three days' duration and was found to have generalized vaccinia. Subsequently the father and two brothers were also admitted to the hospital because of accidental vaccinial infection of the face. All made uneventful recoveries. The mother, who was not affected, was vaccinated in infancy. The rest of the family had never been vaccinated.

Osteochondritis Dissecans in the Army.—Col. Charles M. Marsden and Capt. George Wiernik, R. A. M. C., have analyzed a series of roentgenograms of joints of 18,405 men that were made at the Cambridge Military Hospital, Cambridge, during an eight-year period. The ages of the men ranged from 18 to 30 years. There were 427 cases of osteochondritis dissecans. The diagnostic criterion was evidence ranging from definite localized subchondral decalcification to a chondral or osteochondral loose body or an osteochondral defect in the bone. The knee was the joint most commonly involved (299 cases), followed by the elbow (85 cases), the ankle (35 cases), and the hip (12 cases). The presenting symptom was pain, followed by swelling and instability. Locking episodes were common in the elbows and knees. In these joints arthrotomy for removal of the loose body relieved the locking, but the pain and instability tended to be unaffected. In the ankle, pain was greatly relieved by the removal of the loose body. In the hip, painful limitation of movement in all directions was the presenting symptom in each case. Treatment was palliative. If the lesion does not heal by recalcification or, in more advanced cases, by revascularization with maintenance of the normal contour of the affected bone, a mechanical osteoarthritis of the joint gradually develops.

Fluoridation of Water.—The annual report for 1955 of the Central Health Services Council to the Minister of Health, states that, in two areas in England, one in Wales and one in Scotland, arrangements are now under way for fluoridating the public water supplies at a rate of 1 ppm and for the examination of the teeth of the children in each area before, during, and at the completion of the studies, together with the dental examination of children in control areas. In view of the outcry in certain sections of the community against fluoridation of water supplies, the council devotes much space to the ethical issues involved. By accepting the recommendation that before any general introduction of fluoridation there should be study demonstrations in selected areas, the government has taken steps to insure full opportunity for well-informed opinion to develop.

Poliomyelitis and Housing.—Impressed by the lack of evidence supporting the popular belief that the severer forms of paralytic poliomyelitis tend to be commoner in superior environmental conditions, I. N. Sutherland (*Health Bulletin* 14:52, 1956) has studied the incidence of poliomyelitis in Scotland with respect to the number of rooms and the number of persons per household of victims. Superior households were those with relatively few persons living in a relatively large number of rooms. His figures fail to produce any evidence to support the contention that a superior household environment is associated with a higher incidence of paralytic or nonparalytic poliomyelitis. In the period 1950-1953, the rate per 100,000 population for paralytic poliomyelitis in one-room houses was 18.4 when there were three or less occupants and 69.4 when there were seven or more occupants. In houses containing five rooms or more, the comparable figures were 7.8 and 43.8 respectively. For the same period the rate for nonparalytic poliomyelitis was 5 in one-room houses with three or less occupants, 40 in those with seven or more occupants; 0.8 in houses with five or more rooms with three or less occupants, and 19.7 in those with seven or more occupants.

Psychological Factors in Pulmonary Tuberculosis.—The importance of psychological factors in pulmonary tuberculosis was investigated by D. M. Kissen (*Health Bulletin* 14:44, 1956) in 267 patients attending a diagnostic chest clinic for the first time. Subsequently, and unknown to Kissen until after he had comcompleted his investigation, 88 of these patients were given diagnoses of pulmonary tuberculosis. The remaining 179 patients were used as controls and subdivided as follows: 20 had some form of psychosomatic disease; 68 had no discoverable abnormality; and the remaining 91 patients had miscellaneous conditions. Antecedent emotional factors were found more frequently in the group with pulmonary tuberculosis than in the controls (65.4 and 26.2% respectively). This significantly higher incidence for tuberculosis still held true when compared with the subgroup with no abnormalities (23.5%) and the heterogeneous group (22%), but not when compared with the psychosomatic group (55%). The most common factor was a break or a serious threat of a break in an engagement or a marriage. Other factors were family bereavement or breaks in the family circle. However, the types of emotional factors in the psychosomatic group could not be described as broken love links. There was a significantly higher incidence of emotional factors in tuberculous patients over the age of 35.

This characteristic emotional factor suggested that these patients were especially in need of love or affection. It was therefore decided to investigate this point in a further 45 patients attending the chest clinic for the first time; 20 of these turned out to have tuberculosis, and the other 25 were treated as controls. All 20 tuberculous patients, but only four of the controls, were found to have this characteristic personality trait. Deprivation of natural parental affection was found in 12 (60%) of the tuberculous patients, compared with only four (16%) of the controls. This suggests that the combination of a break in the love link and an inordinate need for affection strongly predisposes to the development of pulmonary tuberculosis.

Sports Injuries.—Of all types of accident in the Royal Air Force, sports account for 28% (*Proceedings of the Royal Society of Medicine*). Because more than 90% of these are due to football, a group of football players will be given special exercises to strengthen their leg muscles. Their experiences will be compared with those of players not so trained. Athletics produce a surprising number of casualties, principally of the ankle ligaments and tendo calcaneus. Dr. W. D. Fletcher states that interference with the higher intellectual function can occur after one bout of boxing; 5% of those who remain in boxing five years become punch-drunk.

Naturopath Sentenced.—Brown Neil, a naturopath, was found guilty of trying to obtain $1,400 by false pretenses from an elderly woman and sentenced to two years' imprisonment. The prosecution said Neil had pretended that a Dr. Franz Schwartz, then living in the United States, had diagnosed Mrs. Swift's condition as cancer in the blood. Neil claimed he had power to treat and cure Mrs. Swift with the aid of equipment called the supersonic pulsator. Mrs. Swift received an unsolicited letter postmarked North Hollywood, Calif., and purportedly written by Dr. Schwartz's secretary. Among statements in the letter were that Dr. Schwartz was still busy supervising the treatment of President Eisenhower; that he had treated a member of the Royal family, who in addition to paying a fee of $2,800 had given a further $42,000 to help poor patients; that on Feb. 15 he had sent his assistant under hypnotic influence to Mrs. Swift's home; and that the assistant examined her sleeping body and found her to have a malignant neoplasm. The treatment was to be by broadcasting from the United States and England by wave-producing instruments. The letter ended by saying that the writer had asked Dr. Brown Neil, of Bournemouth, to treat Mrs. Swift under Dr. Schwartz's direction. In another letter received by Mrs. Swift at the same time signed "Dr. Johnson, M.D.," it was requested that payment for treatment be made by $1,400 in notes. These should be wrapped in brown paper and given to Dr. Neil. Mrs. Swift testified that she was in good health; that she had never heard of Dr. Schwartz; that she took the letters to her solicitor and, on police instructions, wrote to Neil for an appointment; and that she saw Neil on March 20. At her request, he took the brown paper parcel from her shopping bag but put it back when police officers entered. Neil told the police that he did not know Dr. Schwartz, but later he said: "If it will help you, I am Dr. Schwartz." After the trial Mr. A. Samuels, representing the British Naturopathic Association, Ltd., denied that Neil was a member of the association.

A Pathologist's Pay.—The following excerpt from a letter appears in the *British Medical Journal* of Aug. 4 and is quoted to show one aspect of the present-day relationship between medicine and other forms of livelihood. "I wished to become a pathologist when I qualified in 1952, but found that at no time in the ensuing seven or eight years was I likely to earn $2,800 per annum. I therefore entered the family business, where I pay a good representative over $2,800 per annum, plus car, plus expenses. Our travellers have no technical training and their only qualification is that they can sell our goods. It seems altogether wrong that if I were to offer them the salary of a doctor with higher qualifications . . . they would leave forthwith. Most young men qualifying in medicine desire to get married, have a home, a family, security, and freedom from debt. . . . What hope have they got of obtaining luxuries like a car, a television set, or a public school education for the children? I would have preferred to earn my living in my profession, but I wished to marry and felt that I owed my family a minimum standard of living. . . . Worse still, there was . . . little hope for the future, for even if I had higher qualifications what chance had I of obtaining a consultant's post?"

CORRESPONDENCE

WHIPLASH INJURIES

To the Editor:—I would like to comment on the paper by Gotten entitled "Whiplash Injuries" that appears in this issue on page 865, for which the clinical studies have been so well planned and executed. The author and his colleagues deserve a sincere compliment for having presented these facts concerning whiplash injuries, which are becoming so very common. It was three years ago that Dr. Gay and I presented before the Section on Nervous and Mental Diseases a small series of patients (50) with the whiplash injury syndrome. We had attempted to analyze this group and present certain clinical facts that characterized this traumatic syndrome and its subsequent course. Briefly, the syndrome of various aches, pains, and soreness was shown to be due to an acute injury to the cervical musculoligamentous structures and occasionally also due to injuries to the cervical neuroskeletal elements. Although the injury was incurred by several mechanisms, it was most frequently incurred when an auto was struck from behind and the occupant's head, acting as a semi-freely movable object, was suddenly hyperextended and subsequently less violently flexed (see figure). A second phase of this problem, which was strongly emphasized, was what might be termed the "iatrogenic phase." It was shown that the symptoms may be prolonged for weeks to years by ill-advised therapy, or lack of therapy, as handled by various types of medical regimens, physicians, osteopaths, and chiropractors. This, we felt, was an important aspect of the problem, from both the physical and the emotional or psychiatric approaches. Too often, the patient was conditioned for anxiety and tension. This state was developed either by the physician's lack of concern or through an overly anxious and solicitous attitude on his part. When the latter was evident, it suggested to the patient that a serious injury had occurred to his neck and that he would need extensive treatment. Usually this approach was followed by overtreatment, many times including what we believe is the ill-advised rigid fixation of head and neck.

We were able to show that some 70% of our patients displayed a psychoneurotic overlay. Most of these neurotic states or reactions were those of severe anxiety and tension. A further review of this original group, along with another series now comprising some 174 patients presently under study, has shown this to be true. In addition, we have seen reactive depressions appearing in some patients whose symptoms have continued to harass them for months or even years. We have recognized that a prolonged nervous tension state and a fear of (1) pain, (2) serious injury to the neck, and (3) paralysis tends to force the patient to hold his head rigid; in doing so, the patient ironically induces pain, soreness, and aching in the posterior cervical, suboccipital, and shoulder areas. Thus are perpetuated the common symptoms of a whiplash injury.

Before going on to the next point, I should note here that other symptoms of the whiplash injury syndrome may well be compared to the cerebral concussion state. In this syndrome, emotional disturbances are commonly known to perpetuate the symptoms (dizziness, giddiness, headaches, and syncopal-like states) that may be characteristic of the cerebral (cerebroscalp) vasomotor imbalance state. We believe that many of these patients with whiplash injuries have had mild cerebral concussions and that emotional factors play the same role here in perpetuating these symptoms.

Soon after our paper was read before the Section on Nervous and Mental Diseases, Dr. Von Hagen began to gently urge that we study the third phase (phase one being the patient's primary emotional reaction to the injury and subsequent symptoms; phase two, his reaction to his physician's attitude and therapy; and the third phase, the patient's reaction to the legal aspects of his injury. Was there such a reaction? If so, was it adverse in relation to his recovery? What happened to him after this (third) phase was removed?

As we had more experience with these patients and their legal problems, we came to recognize that litigation was, is, and always will be a serious factor in the course and therapy of these patients. At one time we attempted to ascertain how many of 110 patients with whiplash injuries had (1) employed legal aid, (2) litigation pending, and (3) litigation settled. This was done by a mailed questionnaire. The response proved to be most unsatisfactory, for only about a dozen answered this question, among some 15 questions asked, whereas all answered the questions about their symptoms! At the present time, we have under way (in its beginning) a program to have a young psychiatrist review some 225 cases. We hope to have, in another year, some data with which to answer many of these questions.

In the meantime, Dr. Gotten has brought to us irrefutable data concerning this third phase. He has accepted that there is such a syndrome as the whiplash injury syndrome and has shown the strong influence that litigation exerts on the ultimate clinical course of these patients. He has emphasized the monetary phase of this aspect and has not neglected the other aspects of this phase. I should like to draw attention to one facet of this "injury-litigation" problem that is seldom mentioned. Many patients have a fear of legal matters, particularly of "going to court." Of course, this is the fear of the unknown or unfamiliar. But this is just as real as the fear he also holds (1) that no punishment will be meted out to the driver of the other car (and these people do exhibit extreme hostility toward the driver of the other car) and (2) that no compensation will be received for the pain, anxiety, and loss of time that they have experienced. I have seen these patients, after the matter of litigation has been settled, relax and recover even though the legal decision was not in their favor. In these instances, the fear of the court procedure was as real and emotionally and physically decompensating to them as was the injury itself. I would suggest, therefore, that this aspect of the third phase be remembered.

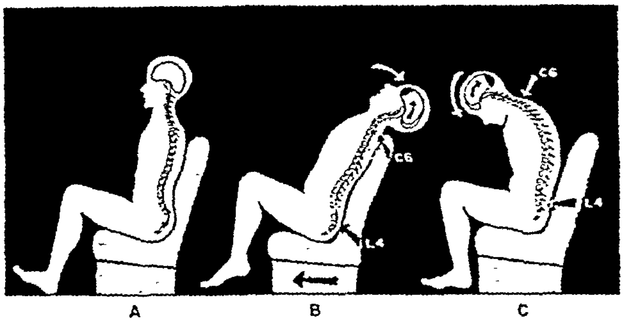


Diagram representing direction of head when vehicle is struck from behind and head is originally directed directly forward. Primary snap of head with greatest force is posteriorly (98% of 214 patients surveyed). Secondary movement is forward. Primary movement usually carries greatest force. However, if the vehicle hit is forced into an object in front at the right time, the secondary movement may be quite violent. It will be noted there is also force applied in the lower lumbar region. In several instances damage to intervertebral disks at the fourth lumbar level has occurred (three ruptured disks in this series).

Finally, it would seem that we have arrived at the same phase, or stage of progress, concerning whiplash-neck-injury syndromes, as we have with head injuries, particularly in regard to cerebral concussion. We accept that there are such injuries and that their symptoms are aggravated by hostility, anxiety, tension, and other emotional reactions. Finally, in both conditions, the ever-present element of litigation can and does affect the clinical course of these patients. In neither type of patient is it clinically possible to determine where the natural or physical course of the injury should end and where or when the perpetuation of the symptoms, due to the neurotic reaction, begins. Certainly one overlays the other in nearly all such cases, and it may be assumed that, in some, the emotional reaction begins with or immediately after the injury. It is, therefore, evident that we have made considerable progress in our understanding of this syndrome.

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BUSINESS PRACTICE

LIFE INSURANCE FOR THE YOUNG PHYSICIAN

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The young physician today, with a background of schooling, internship, and fellowship in modern medicine, is better prepared to begin his practice than were physicians trained in earlier years. He lacks the dimension of experience, but he has intimate knowledge of the latest techniques that give new promise to all of medicine. The preparation by the young physician for his career has taken a longer period of time than did the training of earlier years; therefore, he is older when he graduates. The graduation of relatively large numbers of medical students who already have families of their own—with all the responsibilities of any other family men—is becoming commonplace. Frequently burdened with debt from training and setting up a practice, many of these young physicians defer establishing long-range family protection plans.

In view of this fact, it is not surprising that one of the earliest important problems that should be considered, namely, the establishment of a life insurance program, has never been discussed with many of them. They are not acquainted with the type of life insurance protection available to them and cannot spare the time to investigate so complicated a subject as life insurance. The informed underwriter is trained to assist his client by first diagnosing with questions and discussion the needs and objectives of the young doctor. Knowing these needs and objectives, he can prescribe the program fitted to the young doctor's requirements in their order of importance and, at the same time, can consult with him concerning the limitations necessary in order to keep the proposed purchase within the available budget. Furthermore, frequent review of these objectives and the policies is important to maintaining and building the ultimate program desired. Shopping for bargains or passing insurance business around on the basis of personal friendship will not contribute toward building a sound, integrated insurance program. Finally, there is no such thing as a correct plan for a certain age or income group; each plan should be tailored to the needs of the individual and the premium outlay he can afford. This article is written in the hope of furnishing certain information about policy forms and of stimulating consideration of how they are adaptable to the needs of the young physician when he is planning his program with a life underwriter.

Plans of Insurance

There are basically three types of life insurance policies: whole life, endowment, and term. Whole-life policies provide for the payment of the face amount of insurance only upon death. Premiums may be payable until death, as is the case under the ordinary-life plan; or they may be payable for some limited period, such as 20 years (or until death, if that occurs within 20 years), as is the case under a limited-payment-life policy. Premiums for limited-payment-life policies are higher than for ordinary-life policies because of the limited period for payment of premiums. Cash values under a limited-payment-life policy are also higher. Under either type of whole-life policy, the cash values increase during the life of the policy. A significant development in this type of insurance is that of the whole-life policy with premiums payable to age 60 or age 65, thus spreading the premium-paying period over those years of greatest anticipated professional activity and earnings.

Whole-life policies will normally be bought when the desire is to provide a reasonably large amount of insurance protection for the premiums paid while cash values accumulate. Cash values can provide protection against emergencies requiring ready cash or can be used at retirement to provide an income for life. The choice of a period during which premiums are to be payable must be made at the time the policy is issued and is often based on the individual's budget and his idea of when his earned income will cease. The ordinary-life plan is popular, since it provides the most whole-life-insurance protection for the lowest annual premiums. Twenty-payment-life and life-paid-up-at-65 plans are also popular.

Endowment policies, such as the 20-year-endowment policy, provide for the payment of the face amount on the endowment maturity date (the 20th policy anniversary for a 20-year endowment) or upon death, if earlier; premiums are usually payable during the whole of the endowment period (or until death). The premiums for endowment policies are higher than for corresponding limited-payment-life policies, since the face amount must certainly be paid by the end of the endowment period. Under the limited-payment-life policies, payment of the face amount is made upon death, which may occur considerably later than the end of the premium-payment period. Cash values available under endowment policies are higher than under corresponding limited-payment-life policies. The endowment plans are bought when the desire is to have a lump sum available on a predetermined date in the future should the insured survive until then. Many endowment policies are bought with a maturity date of age 65 for the purpose of taking an income settlement instead of a lump sum, that is, with the purpose of providing retirement income. Twenty-year endowments are also bought widely, many being purchased for the purpose of setting up an educational fund for a child upon maturity of the policy.

Term policies provide for payment of the face amount only upon death within the term period. Premiums are usually payable during the entire term period (or until death). The protection afforded by a term policy is temporary, with coverage existing only during the term period. Premiums for term policies are lower than for corresponding limited-payment-life policies, and, in most cases, there are no cash values available. Term insurance is usually purchased when the need is a temporary one and is for the largest amount of insurance that can be bought by the premium payable. Frequently the view that the need for insurance is temporary is supplanted by a later realization that permanent insurance is needed. Most term policies provide limited rights of conversion, without medical examination, to the regular permanent plans of insurance. Since these conversion rights are limited, the policy should be carefully studied so that the conversion rights may not be lost by a failure to elect conversion soon enough.

Almost all other plans of insurance can be classified as modifications or combinations of the three basic plans. Some of the more important plans to consider are those of special policies (generally issued only for large amounts) and renewable term policies. Many companies have in recent years introduced a special policy available only to the purchaser who is willing to buy insurance on this particular plan and for at least a minimum amount at which the special policy is issued. (This minimum may, for example, be $10,000.) Some companies offer these special policies only to specially selected or preferred risks. Recently the special policies have figured prominently as competitive items, inasmuch as the issuance of insurance in larger amounts has the effect of reducing the level of unit expenses; and, moreover, the cost of insurance may be further reduced when the policy is restricted to preferred risks. If the young physician has an insurance need that can be met by one of the special policies, he may be well advised to take advantage of the lower rates available under these plans. Some of these special policies offer the privilege of increasing the premiums at an age such as 55 for the purpose of making the policy paid-up or for its maturity as endowment at an age such as 65. Thus they become flexible and are readily adaptable to the larger income that may likely be available for premiums after the period when the normal need for the purchase of additional life insurance in substantial amounts has expired.

A renewable term policy can be best described as a regular term policy that contains an additional feature or benefit. This benefit is the right to renew the policy for another term period (usually without medical examination) at a premium rate guaranteed at the original issuance of the policy. The premium rate increases at each renewal, eventually becoming quite large as compared with the premium at the original age of issue, and

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From the Bureau of Medical Research (Dr. Ungerleider), the Equitable Life Assurance Society of the United States.

ultimately at some age stated in the policy, usually in the middle 60's, it becomes necessary under these forms to discontinue the protection or convert it at the then attained age to the regular whole-life or endowment plans. The right to convert to the regular permanent plans is likewise usually available at the earlier ages, but too frequently in the experience of insurance companies it is not exercised when the higher premium can first be budgeted by the insured.

Important Features of Life Insurance Policies

In addition to the lump-sum death benefits that are available, life insurance policies contain many features that are of considerable value to the insured. One example of such a feature is contained in the beneficiary provision. This gives the insured the right to change his beneficiary at any time. It is also customary to allow the insured to name several persons rather than just one as his beneficiary and to provide that, instead of a lump sum, the death benefit will be held on deposit or will be paid under various installment options. The beneficiary provision provides the insured with certainty that the insurance benefits will be paid out in accordance with his wishes, since the terms of the beneficiary arrangement are carried out by the company as a matter of contract. The practice of private life insurance companies in carrying out such arrangements as a matter of contract contrasts with that under certain government plans, where benefits can terminate after the death of the insured upon occurrence of certain events, such as remarriage of the widow. Certain rights are also guaranteed the insured should he decide at some point after issue of the policy that he no longer wishes to continue making premium payments. The usual benefits available in such an event are a lump-sum payment of the cash value, continuation of protection for the full face amount of insurance for such period as the cash value will provide, or continuation of the policy as a fully paid-up policy for a reduced face amount of insurance providing the same form of benefits as would be available had premiums been continued.

There are many riders for "extra" benefits that may be included in a policy of life insurance. The two most popular provisions are for waiver of premiums in the event of total and permanent disability and for additional indemnity in the event of death by accidental means. The first provides that total and permanent disability, which results in reduction or discontinuance of earned income, will not cause termination of the life insurance policy. The second in its usual form provides for payment of double the face amount if death is caused by accidental means as defined in the provision. The cost of these benefits is small in respect to the premium for the basic policy, so that the majority of life insurance policies issued today contain at least one of these riders.

Family-income riders provide for the payment, commencing upon the death of the insured, of a monthly income until the end of a stated number of years from issue of the policy, with payment of the face amount of insurance at the end of that period. Such a rider might be added to the basic policy by a man recently become a father, with the thought that his family would be provided for by the income benefit until the child had grown up. There would then be a lump sum available that could be used for such purposes as providing a life income for the widow, setting up an educational fund, or helping to set the family up in business. Another purpose for which these riders are frequently used is mortgage redemption. The benefits available, which are of a reducing nature, can be made to correspond very closely to the reducing unpaid balance of a conventional mortgage. The family-income benefit can be purchased at a premium that is low compared to the premium for permanent plans of insurance. It should be remembered that the benefits available become less as the policy stays in force, so that the total benefit under the policy after the end of the family-income period is equal to the face amount. When setting up a program designed to guarantee the basic income needs for a young doctor's family, the use of the family-income rider on certain of the policies allocated to this need furnishes added protection when it is most essential and still leaves the primary policy intact for continuance as protection for the wife after the children are on their own, or even for retirement purposes, assuming the insured's survival to the older ages.

Disability-income riders provide for payment of monthly income usually until age 65 but frequently for life if the insured becomes disabled as defined in the rider. In most cases, the disability must occur before age 60. The amount of the monthly income is most often $10 per $1,000 face amount of insurance, so that a man having a $10,000 policy with this rider attached could collect an income of $100 per month should he become disabled. This benefit is of particular importance to physicians who become so disabled as to be unable to perform their usual duties. The cost of the rider is small in relation to the premium for the basic policy, but the benefits payable for disability occurring early in life are substantial. Frequently, however, the young doctor will consider a somewhat higher, although usually temporary, form of disability-income coverage offered by an accident and health policy instead of having this feature on policies incorporated in his regular life insurance program.

Premium Rates

It should be pointed out that insurance is sold on both a "participating" and a "nonparticipating" basis. Under a participating policy, the premium rate charged is somewhat higher than the premium considered necessary, with the anticipation that the excess premium will be returned in the form of dividends over the years. A nonparticipating policy provides insurance at a set premium rate, with no prospect of any dividend ever being paid. Under the participating policies, various attractive options are available for leaving the dividends with the company and for increasing the protection and cash equities in the policy. The figures shown in the table are illustrative of the premiums charged, the dividends paid currently, and the values contained in policies issued by a company that issues participating insurance. All figures are shown per $1,000 face amount, or, in the case of the family-income riders, per $10 monthly income. Dividends are not guaranteed but will depend on the actual experience over the years.

Illustrative Data on Participating Insurance

Issue Age	Annual Premiums, $	Av. Annual Dividend over 20 Yr., $	Av. Annual Net Outlay, $*	20th Yr. Guaranteed Cash Value, $	Age 65 Guaranteed Cash Value, $
Adjustable Whole Life (Minimum Face Amount $10,000)					
25	17.46	3.86	13.60	287	614
30	20.08	4.32	15.76	326	583
Life Paid-Up at 65					
25	22.49	5.80	16.69	328	764
30	26.36	6.61	19.75	388	764
Endowment at 65					
25	25.49	6.43	19.06	393	1000
30	29.95	7.21	22.74	471	1000
20-Payment Life					
25	32.67	7.07	25.60	559	764
30	35.93	7.75	28.18	610	764
20-Yr. Endowment					
25	50.11	8.58	41.53	1000	...
30	50.87	8.82	42.05	1000	...
5-Yr. Renewable Term (Minimum Face Amount $5,000)					
25	7.95	2.46†	5.49†	...	...
30	8.90	2.85†	6.05†	...	...
20-Yr.-Family-Income Rider					
25	3.92	...	3.92	...	...
30	4.83	...	4.83	...	...
Family-Income-to-Age-65 Rider					
25	11.05	...	11.05	...	...
30	11.60	...	11.60	...	...
Ordinary Life (Sold Only for Amounts $1,000 to $9,999)					
25	20.68	5.57	15.11	287	614
30	23.69	6.29	17.40	326	588

*Premium for 1st 20 yr. less average dividend.
†Averaged over 5 yr.

Let us see how a young physician, say age 30, with a wife and two children, one 2 years old and the other just born, might provide benefits for his family using life insurance. He wishes to provide his family with a maximum of protection while at the same time his policy is accumulating some cash values. This young physician might feel that a combination of one of the special policies for $20,000 with a 20-year-family-income rider would serve his purposes. This combination would provide income to his widow and children of $200 a month in the event aspirin and Demerol for relief of her distressing dyspnea. On this regimen she was able to return home. One month prior to the present admission she noted more rapidly increasing shortness of breath. Another physician noted distended neck veins, cardiomegaly, and pitting edema of the lower extremities. The dyspnea improved greatly with the use of mercurial diuretics and digitalis, although it still confined the patient to bed.

On admission to the District of Columbia General Hospital the patient complained of shortness of breath and pain in the right forearm and breast. Fluoroscopy revealed fair motion of the diaphragm. A mottled increase in density was seen throughout both lungs. This density tended toward confluence in the right lower lung field. Enlargement of the heart, mostly the left ventricle, was also seen. Seven blood cultures remained sterile. Sputum and gastric washings revealed no acid-fast bacilli. After an initial improvement resulting from diuresis, it became apparent that the patient was slowly losing ground. The slightest effort provoked extreme tachypnea. Fever persisted the first week in the hospital and reappeared with the onset of gastrointestinal bleeding. After a blood transfusion she admitted having a mild midepigastric pain intermittently over the preceding month. She described the pain as burning or gnawing and stated that it was sometimes relieved by food. She was placed on a modified ulcer regimen. Her death occurred 28 days after admission to the hospital. A review of the slides of lung tissue that had been obtained at biopsy in September, 1953, revealed changes typical of diffuse interstitial pulmonary fibrosis as described by Hamman and Rich.

This patient's illness was characterized by a slow, relentless loss of pulmonary function. The duration of symptoms was about 20 months. This is a longer duration of symptoms than that in the cases reported by Hamman and Rich. However, recent articles have also reported longer duration, and treatment with hydrocortisone may have prolonged the course of the disease. Cyanosis was not clinically evident, probably because it is difficult to evaluate clinically in the presence of anemia and particularly in Negroes. The gastrointestinal bleeding is interesting, since a duodenal ulcer was reported in other patients with this form of interstitial pulmonary fibrosis. The cause of diffuse interstitial pulmonary fibrosis as described by Hamman and Rich remains unknown. Several authors have speculated as to a virus etiology or some relation to the collagen diseases. That an altered state of tissue reactivity is present seems to be a reasonable assumption.

The Chemotherapy of Peripheral Tuberculous Lymphadenitis. O. H. Friedman and I. J. Selikoff. J. Mt. Sinai Hosp. 23:529-536 (July-Aug.) 1956 [New York].

Friedman and Selikoff present observations on 44 patients with peripheral tuberculous lymphadenitis who were treated during the past four years at the Mount Sinai Hospital in New York, N. Y. The generalized nature of tuberculous lymphadenitis must be appreciated, whether the local lesion is the result of a primary tuberculous infection or of a lymphohematogenous postprimary dissemination. Recent studies indicate that in the former case disseminated organ tuberculosis (pulmonary, meningeal, pleural, osseous) not infrequently follows the appearance of primary infection with local lymphadenitis. When peripheral tuberculous lymphadenitis is part of a postprimary lymphohematogenous dissemination, evidence of disseminated tuberculosis is often found in other organs. In view of this generalized nature, chemotherapy is necessary for every patient with active tuberculous peripheral lymphadenitis. Local therapy, such as excision, radiotherapy, and antimicrobial injections, may be useful as accessory treatment for the local lesion. Isoniazid alone or in combination with other antituberculous drugs is the treatment of choice. Data are still inadequate for the selection of an optimum regimen, but any chemotherapeutic regimen containing isoniazid will yield a high percentage of satisfactory results.

Chemotherapy must be prolonged; a minimum of one year is required. Short-term chemotherapy carries a risk of inadequate response and/or recurrence of disease. If there is a recurrence, it is usually in the same area as the original lesion. Response to chemotherapy is noted soon after its institution. Should no effect on the local lesions be noted in four months, the diagnosis of peripheral tuberculous lymphadenitis should be reviewed. Maximum response, however, requires a much longer period, and chemotherapy should be continued until it has been obtained and has remained stable for at least four months. Since peripheral tuberculous lymphadenitis is a chronic and relapsing disease, the patient must be kept under observation for a long time even after chemotherapy has been discontinued.

Treatment of Human Tuberculosis with Cycloserine. A. Ravina and M. Pestel. Presse méd. 64:1241-1245 (July 4) 1956 (In French) [Paris, France].

The authors report results of clinical experiments on 80 tuberculous patients treated with Cycloserine for 10 months. They recorded from 60 to 75% unquestionable improvement in subjects who were affected by chronic ulcerative cavitary processes and who were no longer responsive to other antibiotics. They also observed some rapid regressions in the cases of recent ulcerating, infiltrating processes. The daily dosage of Cycloserine was 2 capsules of 250 mg. initially, with gradual increase up to 5 capsules. The mechanism of action of the drug seems to differ from that of isoniazid and streptomycin. Cycloserine is slow to produce results at first but has a prolonged effect apt to continue for months. So far there is no clinical or experimental evidence of any eventual resistance of the bacillus to this medicament. A combination of Cycloserine and isoniazid proved remarkably effective in a large number of cases. It allowed the dosage of Cycloserine to be lowered and made it better tolerated. There were 12 instances of side-effects, chiefly of psychomotor type. Five of these were epileptic in nature. The authors emphasize the importance of a careful preliminary examination of the patients with a view to eliminating persons with psychotic symptoms and those with a history of epilepsy. They used encephalograms systematically after starting the treatment and in addition had the patients examined clinically to detect signs that would indicate that the treatment should be discontinued at least temporarily (irritability, change in humor, paradoxical asthenia, somnolence). Since Cycloserine is less manageable than isoniazid, its administration requires close supervision during the first weeks; consequently, its use should be carried out in medical establishments. Cycloserine is an additive antituberculous agent rather than a replacement for streptomycin, isoniazid, and *p*-aminosalicylic acid.

Drug Therapy (Mecamylamine) of Hypertension: III. Results with Mecamylamine, a Completely Absorbed Ganglionic Blocking Agent. J. H. Moyer, R. Ford, E. Dennis and others. A. M. A. Arch. Int. Med. 98:187-210 (Aug.) 1956 [Chicago].

Ganglionic blocking agents appear to be the most potent therapeutic agents for reducing the blood pressure in patients with severe hypertension. Recently another long-acting ganglionic blocking agent has become available for clinical trial. This compound, mecamylamine, is a secondary amine (rather than a quaternary compound) which is completely absorbed from the gastrointestinal tract. The authors describe observations on 104 patients from the hypertension clinics of several hospitals. The majority of these patients were treated entirely on an outpatient basis, but in a few patients with severe disease, such as hypertension associated with encephalopathy and cardiac failure, it was necessary to initiate therapy in the hospital. Twenty-four patients received mecamylamine alone, and 80 patients received mecamylamine and Rauwolfia together. The patients who received mecamylamine and Rauwolfia in combination responded more satisfactorily as a group when compared with the patients who received mecamylamine alone. Although mecamylamine appears to be an effective drug for reducing the blood pressure in patients with severe hypertension, certain problems arise in the management of these patients. It is particularly difficult to adjust the dose exactly so that the blood pressure remains stable throughout a 24-hour period. While some patients obtained an adequate response on a dose of 2.5 mg. of mecamylamine given twice a day, some patients required as much as 160 mg. per day. The use of an average dose is impossible and will lead to an intolerable incidence of complications. Some patients showed a very marked reduction in blood pressure in the upright position, with considerably less response in the supine position. The authors found it impossible to overcome this problem. Some patients displayed a marked early morning reactivity due to mecamylamine. In these patients it became necessary to reduce the night-time dose or, in many instances, discontinue it completely. Also, these patients required a relatively small breakfast dose.

The dosage of mecamylamine when given in combination with Rauwolfia is frequently less than when mecamylamine is used alone, and, as a consequence, there is less blockade of the parasympathetic nervous system. This reduces the severity of the side-effects resulting from blockade of this system, i. e., constipation, dry mouth, and blurred vision. Constipation is one of the most constant side-effects of mecamylamine therapy. If this problem is not combated vigorously, it may lead to fecal impaction and subsequently to ileus. If the constipation has progressed to ileus before adequate therapy is instituted, then the mecamylamine should be discontinued and 1 mg. of neostigmine should be given parenterally every hour until relief is obtained. If the condition is severe, standard methods for treating ileus should be employed. The possibility of aggravating a preexisting renal failure presents another problem. If the blood urea nitrogen level is above 80 to 100 mg. per 100 cc. of blood prior to therapy, reducing the blood pressure significantly usually aggravates the renal failure. If, however, the blood urea nitrogen level is only moderately elevated (40 to 60 mg. per 100 cc.), then judicious lowering of the blood pressure with a ganglionic blocking agent such as mecamylamine can be undertaken. In treating the patient who is considered a hypersensitive emergency, particularly if he is bedfast, it is usually better to administer reserpine parenterally as the initial procedure (rather than a ganglionic blocking agent).

The Role of Sulphonylurea Derivatives in the Management of Diabetes Mellitus: A Preliminary Report. E. Downie, J. Bornstein, B. Hudson and K. Taylor. M. J. Australia. 1:1072-1078 (June 30) 1956 [Sydney, Australia].

The mode of action of the sulfonylurea compounds upon the disturbed metabolic processes of diabetes mellitus is unknown. Although they seem to have the effect of lowering the level of blood sugar and of reducing the excretion of glucose by the kidneys in some patients, it cannot be assumed that these results are achieved by an action similar to that of insulin; in fact, they cannot be regarded as insulin substitutes. Janbon and his associates reported that *p*-amino-benzene-sulphonamido-isopropyl-thiadiazole reduced the blood sugar content of animals to hypoglycemic levels. Another sulfonamide derivative, 1-butyl-3-p-amino-benzene-sulfonylurea (BZ-55 or Carbutamide), and 1-butyl-3-p-toluene-sulfonylurea (Orinase) have also been shown to possess hypoglycemic activity. Carbutamide lowers the level of blood sugar, reduces glycosuria, and in some cases may replace insulin therapy. Success has been reported in clinical trials of the drug. It seems that the middle-aged obese patient responds satisfactorily to its use, but the young patient and the "brittle" one are uninfluenced, even by large doses. Experiments in animals have failed to show any serious side-effects from the administration of these drugs, even in high doses over long periods of time. In rare instances human patients have developed leukopenia, which has disappeared with a reduction in dosage of the drug. The failure of some patients whose plasma contains appreciable amounts of insulin to respond favorably to treatment with sulfonylurea compounds suggest that these drugs do not act by facilitating insulin action. It seems unlikely that they improve the condition of insulin-resistant patients who have demonstrable insulin in their plasma. At the present time there is potential danger in the indiscriminate use of these compounds, and further experience is necessary before their place in the treatment of diabetes mellitus can be determined.

Eosinophilic Leukemia. G. Cave Bondi and A. Lenzini. Sett. Med. 44:294-303 (June 15) 1956 (In Italian) [Florence, Italy].

The authors report the case of a 21-year-old patient with eosinophilic leukemic myelosis. The history of the patient showed no previous disease. The general condition of the patient was good when he underwent a medical checkup because of a feeling of heaviness in the left hypochondrium. A marked splenomegaly was found. All tests gave normal results except the hemocytometric test, which showed an increase of white corpuscles. Splenectomy was performed. The operation showed that there was no echinococcosis of the spleen. No improvement followed the operation. Two weeks after the intervention the white blood cell count reached 88,000. At the same time immature forms appeared in the circulation and the myelogram showed eosinophilic metaplasia in the bone marrow. Two months later the patient suffered a severe exacerbation of the leukemia with deep oropharyngeal ulcerations. Various therapeutic measures had little or no effect on the course of the disease. Ethylurethane given in doses of 3 gm. per day for three weeks had no effect. Cortisone and ACTH had no effect. A slight improvement followed treatment with Cloronaftina, a proprietary preparation of bis (2-chloroethyl) naphthamine.

The Incidence of Blood Group A in Pernicious Anemia. W. P. Creger and A. T. Sortor. A. M. A. Arch. Int. Med. 98:136-141 (Aug.) 1956 [Chicago].

Since the incidence of blood group A is significantly higher in patients with cancer of the stomach than in the general population, and since cancer of the stomach is three or four times as common in pernicious anemia as in the population at large, the incidence of blood group A in pernicious anemia seemed of some interest. Patient records that had been filed under the heading "pernicious anemia" at the Stanford University Hospitals (1937-1955), the University of California Hospital (1934-1955), and the San Francisco Hospital (1942-1954) were examined. Of 524 records that had been filed under the heading "pernicious anemia" at the three institutions, 115 contained a blood group determination and also satisfied the diagnostic criteria sufficiently to be regarded as representing cases of pernicious anemia. The blood group distribution of 20,070 donors provided control values. The percentage of persons who were group A was 35% higher in the cases of pernicious anemia than in the normal blood donors. The significance of the observed higher incidence of blood group A in pernicious anemia is shown not to be identical with that of the characteristic hair and eye color and ethnic origin of persons with this disorder. The increased incidence of blood group A in pernicious anemia as demonstrated in this report, and the previously reported increased incidence of the same blood group in gastric cancer, is interpreted as suggesting that both gastric cancer and pernicious anemia may be related to the occurrence of blood group A rather than being directly related to each other.

Paroxysmal Nocturnal Hemoglobinuria: Case Study, Including Evidence of Affection of the Marrow in the Disease. A. M. Nussey and D. W. Dawson. Blood 11:757-763 (Aug.) 1956 [New York].

A case of fatal paroxysmal nocturnal hemoglobinuria in a 65-year-old woman is described. The patient had bouts of abdominal pain coinciding with the frequent passage of dark urine. These bouts lasted for periods of up to two weeks at a time, with intervals of days or weeks between. Her condition was recognized when, after passing more than usually blood-stained urine, she looked very pale and showed a hemoglobin level of 5.2 gm. per 100 cc. The tip of the spleen could just be felt, but otherwise there was no noteworthy abnormality. Prolonged observation of the patient's urine confirmed the intensification of hemoglobinuria after a night's sleep and an unpredictable variation in its incidence from one week to another. The patient received cortisone for two and a half months, and this may have slowed down very slightly the drop in the patient's hemoglobin. The only treatment of proved value is blood transfusion, and the patient received 34 pt. of blood over a period of five years. If she went without transfusion for any length of time, her hemoglobin tended to find a level of about 5 gm. per 100 cc. and to stay at that point no matter how long the interval. This may mean either that the patient's marrow could keep production up to this level or that a proportion of her morphological blood elements were resistant to the hemolytic system.

Van den Bergh's finding that hemolysis in paroxysmal nocturnal hemoglobinuria is enhanced by increased acidity was confirmed, since all the morphological blood elements of the patient became lysed when suspended in acidified serum. There were no obvious incidents of thrombosis before the patient's final illness. A sudden onset of generalized headache and vomiting, drowsiness, and photophobia suggested the occurrence of venous cerebral thrombosis, but the recovery of xanthochromic cerebrospinal fluid on lumbar puncture was thought to favor the occurrence of a subarachnoid hemorrhage, and anticoagulants were therefore withheld. After a short-lived improvement the patient sank into a coma and died. Autopsy showed an extensive cerebral venous thrombosis and an old thrombotic lesion in the spleen and another in one adrenal. The mode of her death exemplified clearly the peril in which such patients stand from their thrombotic tendency. The abundance of iron in the patient's kidneys was in accordance with the general findings in paroxysmal nocturnal hemoglobinuria. The hemosiderosis in the liver, spleen, and an abdominal lymph node was probably caused in her case by the numerous transfusions she had received. The marrow of the sternum was hypocellular, and that of the ribs was aplastic. It seems reasonable to assume that in paroxysmal nocturnal hemoglobinuria the state of the marrow reflects not only the level of anemia but also the local activity of the hemolytic system, a hypercellular marrow showing a better capacity for coping with the disease than a less cellular marrow. The concept that the marrow in this disease is exposed to the action of the hemolytic system would explain why it does not rise to such regenerative heights as in congenital spherocytosis.

Newer Concepts of the Pathogenesis of Idiopathic Thrombocytopenic Purpura. C. V. Moore. Cincinnati J. Med. 37:295-299 (Aug.) 1956 [Cincinnati].

The results of studies carried out in patients with idiopathic thrombocytopenic purpura at the Washington University School of Medicine in St. Louis suggest that idiopathic thrombocytopenic purpura is a syndrome rather than a specific disease entity. In many patients, an immunologic mechanism seems to be of pathogenic importance, causing both accelerated destruction of platelets and damage to megakaryocytes. The thrombocytopenic, immunologic factor appears to be a platelet agglutinin. In 12 patients the antiplatelet factor was not demonstrated. It is suggested that in these patients a different mechanism was involved, and that inadequate production of platelets alone may be responsible for the thrombocytopenia.

The spleen apparently participates in the removal of sensitized platelets from the circulation, and probably produces some of the platelet agglutinin. This concept is supported by the following observations. After the injection of human plasma known to contain a high titer of platelet agglutinins, given to both a normal and a splenectomized recipient, the platelet level was lowered in both. However, when plasma with a low titer of platelet agglutinins was injected into two similar recipients, the platelets decreased only in the normal person; no lowering of the count occurred in the splenectomized patient. Splenectomy was performed on 20 patients with platelet agglutinins in their plasma. Fourteen responded to the operation, and six did not. Failure of splenectomy to correct the thrombocytopenia may be caused by the persistence of a high titer of platelet agglutinins after the operation. Another possibility that may be considered is that the spleen is of lesser importance in the production of thrombocytopenia in those patients who do not have platelet antibodies. Neonatal thrombocytopenia may develop from placental transmission of autoagglutinins or isoagglutinins.

Hageman Factor (HF) Deficiency. B. Ramot, K. Singer, P. Heller and H. J. Zimmerman. Blood 11:745-752 (Aug.) 1956 [New York].

Hageman factor deficiency was described for the first time in 1955 as a familial characteristic associated with deficiency of a clot-promoting fraction of plasma to which the name of the first patient in whom the newly discovered disorder was recognized was applied as an eponym. Hageman factor deficiency is a syndrome characterized by the complete absence of any hemorrhagic tendency in the presence of laboratory findings that, as a rule, are associated with severe disturbances in the hemostatic mechanism. The authors describe an additional case of this syndrome in a 60-year-old man of Lithuanian descent. He came to the United States at an early age and did not know anything about his parents or siblings. His two children and two grandchildren did not have any clotting abnormality. The patient was admitted to the Westside Veterans Administration Hospital in Chicago for the removal of large varicose veins. The results of all routine laboratory tests of his urine and blood were within normal limits except for a markedly prolonged clotting time of more than 60 minutes. The plasma prothrombin time was normal, but prothrombin consumption was decreased. The thromboplastin generation test according to Biggs and Douglas' technique revealed that Hageman factor is essential for blood thromboplastin formation at least in vitro. This test and additional studies made it possible to differentiate the patient's Hageman factor deficiency from similar "hemophilic syndromes" caused by lack of antihemophilic factor (AHF), or plasma thromboplastin component (PTC) or plasma thromboplastin antecedent (PTA). Transfusions of 50 cc. of 20-day-old blood rapidly restored the patient's clotting and serum prothrombin times to normal; the thromboplastin generation also became rapidly normal. This corrective effect was maintained for about 36 hours. Extremely minute amounts of Hageman factor seem to be necessary to normalize thromboplastin formation. The lack of spontaneous bleeding in fully developed Hageman factor deficiency and in plasma-thromboplastin-antecedent deficiency also suggests that these two factors are not essential in the maintenance of the physiological "integrity" of the vascular wall. Since any transfusion carries some risk, it is of practical importance to emphasize the fact that preoperative preparation with transfusions can be omitted in patients with Hageman factor deficiency.

Systemic Lupus Erythematosus: Recent Advances in Its Diagnosis and Treatment. E. L. Dubois. Ann. Int. Med. 45:163-184 (Aug.) 1956 [Lancaster, Pa.].

One hundred forty-five female and 18 male patients between the ages of 1 and 69 years with systemic lupus erythematosus were treated at the Los Angeles County General Hospital between 1948 and 1955. The apparently increasing incidence of this disease during the six-year period is a result of the more frequent use of the lupus erythematosus (L.E.) cell test and of a more inclusive concept of systemic lupus erythematosus, which is a chronic disease resembling rheumatoid arthritis. Part of the rising incidence may also be due to the perfecting of more sensitive techniques of L.E. cell detection.

Simultaneous L.E. cell studies were performed on 44 patients with systemic lupus erythematosus by four different methods, the use of two concentrations of heparin as an anticoagulant, a clotted method, and the recent Snapper ring technique. In 10 patients the clotted method was the only test that yielded positive results; in 4 patients the ring technique was the only one that gave positive results, and in two patients the heparinized specimen was the only positive one. With increasing amounts of heparin fewer L.E. cells were found. It is advisable that at least three different types of L.E. cell tests be performed to screen a suspected case adequately. Despite these refinements, L.E. cells may not be found in all patients with systemic lupus erythematosus.

The study of the histories of the 163 patients gave the best concept of the course of the illness. Sixty-three patients (38.7%) had spontaneous remissions before any special therapy was instituted. Ten patients (6.1%) had at least two remissions, and 26 (16%) had multiple remissions. This makes evaluation of therapy difficult, especially as none of the therapeutic agents used is specific and some may be hazardous. Bed rest alone is helpful in controlling symptoms in the active stages of the disease, but if a remission does not ensue after several weeks of rest more vigorous therapy should be instituted. If salicylates and rest fail, or if cutaneous lesions are present, then antimalarial drugs should be given. Quinacrine (Atabrine) hydrochloride, chloroquine phosphate, or amodiaquin hydrochloride were given to 134 patients with milder cases of the disease. The effect of these drugs on the cutaneous lesions was almost specific. The arthritis was also greatly benefited. Eighty per cent of the patients were benefited by antimalarial agents alone. One hundred seven (90%) of 132 acutely ill patients who were given a first course of steroid therapy were benefited. Daily doses of 300 mg. of cortisone, 240 mg. of Hydrocortone, or 40 mg. of prednisone or prednisolone were usually given before the illness was brought under control.

Steroid therapy is still the mainstay of treatment in the acutely ill patient, but its synergistic use with antimalarial drugs may often reduce the steroid dose and may occasionally permit discontinuation of steroid therapy. Nitrogen mustards were given to 33 patients who received 48 courses of methyl-bis (beta-chloroethyl) amine hydrochloride by intravenous route and 11 courses of triethylene melamine orally. The latter drug was discarded because of its toxicity. The most pronounced effects of nitrogen mustard therapy occurred in the edematous nephrotic patients with systemic lupus erythematosus in whom a marked diuresis developed within from a few days to two weeks after receiving the drug. Patients with active systemic lupus erythematosus without renal damage were not benefited by this treatment. These methods of treatment prolonged the lives of the patients. The median duration of life of 59 untreated or inadequately treated patients with systemic lupus erythematosus was 24 months. Only 33 of the 138 adequately treated patients with a duration of 24 months or longer of their disease, i. e., less than 10%, have died; this difference is significant.

Survival in Untreated and Treated Cancer. M. B. Shimkin, M. H. Griswold and S. J. Cutler. Ann. Int. Med. 45:255-267 (Aug.) 1956 [Lancaster, Pa.].

The cancer record register of the State of Connecticut, which has been in operation since 1935, most closely answers the requirements for a source of data from which estimates of survival with cancer among the general population can be derived. Between 1935 and 1951, 75,494 cases of cancer were diagnosed among the inhabitants of Connecticut, of whom there were two million in 1950. The five-year survival of male patients increased gradually from 12% between 1935 and 1940 to 20% between 1947 and 1951. For female patients the comparable increase was from 19% to 32%. This improvement in the survival rate did not result from earlier diagnosis of the cases, since there was no consistent or significant change in the distribution of localized and disseminated cases during the entire period of study. The improvement in the survival rate of patients with cancer occurred in those in whom the diagnosis was made when the cancer was clinically localized and when it involved regional areas, but not when it was disseminated. The most marked improvement in the survival rate has been recorded for cancer of the colon and rectum in patients of both sexes and of the uterine cervix in women. These data were compared with those of anticipated survival in patients with untreated neoplastic disease. The improvement in the survival rate seems to be the result of increasingly better treatment of an increasingly greater proportion of the patients. A new era of detection and treatment of cancer is being entered upon as a result of studies on in situ and occult cancers among the general population.

Salt-Losing Nephritis: Review and Report of a Case. A. H. Levere and L. G. Wesson Jr. New England J. Med. 255:373-376 (Aug. 23) 1956 [Boston].

The history of salt-losing nephritis is briefly presented and an additional case is described. The patient was a 29-year-old man who complained of weakness, nausea, and vomiting. Five weeks before his admission he began to experience aching and cramps in his limbs, accompanied or soon followed by nausea and vomiting without hematemesis and usually while he was riding in vehicles. He also noticed weakness, fatigue, exertional dyspnea, increasing thirst and polyuria, and a loss of 2.3 kg. (5 lb.) in weight. His condition deteriorated rapidly, although therapy for chronic renal disease was instituted. An electrocardiogram revealed prominent peaked T waves. The plasma potassium level at this time was 7.6 mEq. per liter. He became lethargic, had marked nausea, and vomited. He appeared better after an infusion of isotonic sodium chloride solution given in an attempt to correct suspected dehydration. Because of this, and the evidence of increased urinary excretion of sodium concomitant with a high degree of renal insufficiency, it was suspected that he had a salt-losing type of renal dysfunction. After he was treated for this condition he improved, and he was discharged after 68 days in the hospital.

After discharge he adhered to a low-protein diet with from 6 to 10 gm. of supplementary salt and 3 gm. of calcium lactate daily, returning regularly to the outpatient clinic for follow-up examination. Except for occasional calf and thigh cramps, he is relatively asymptomatic. Two needle biopsies were performed on the right kidney: the first revealed infiltration of the interstitial tissue by chronic inflammatory cells. The tubules showed extensive degeneration. Some of the six glomeruli observed showed irregular thickening of the basement membranes of the tufts and more marked thickening of the basement membrane of Bowman's capsule. The second biopsy revealed changes similar to those noted in the first specimen. Thickening of the basement membranes was present, supporting glomerulonephritis as the most probable pathological diagnosis. The degree of membrane thickening, however, is too mild to permit this diagnosis to be established beyond doubt.

Hyponatremia in the presence of a urine rich in sodium chloride is recognized also in Addison's disease. Salt-losing nephritis has many features in common with Addison's disease. It differs principally in that the defect in tubular sodium chloride reabsorption is organic, a consequence of renal disease, and hence irreversible by steroid administration. Hyponatremia with excessive renal salt loss has been recognized in certain patients with pneumonia, congestive heart failure, peritonitis, tuberculous meningitis, and particularly pulmonary tuberculosis. The inability of the kidneys to conserve salt efficiently is usual in chronic renal disease, although the loss of amounts sufficient to cause symptoms that dominate the clinical picture and simulate adrenocortical insufficiency is rare. It is not unusual, however, to observe that patients with chronic nephritis who have been placed on a low-salt diet to control edema formation may become somewhat dehydrated and then show a striking improvement when 1 to 5 gm. of salt is restored to the diet. It is likely, nevertheless, that salt-losing nephritis is a particular variant of chronic Bright's disease that differs from the more usual forms in more respects than a simple quantitative increase in the amount of salt lost in the urine. Therefore, the authors propose certain minimum criteria that should be met for the diagnosis of salt-losing nephritis as distinct from other salt-losing states: signs and symptoms consistent with dehydration are present on a normal salt intake (5 to 8 gm. per day) and can be relieved by an intake of 10 to 20 gm. of salt per day; the clinical state cannot be relieved by desoxycorticosterone acetate or, alternatively, steroids are present in the urine in normal amounts; and evidence of renal disease is present (low specific gravity, polyuria, elevated plasma urea and creatinine and anemia) and persists on high-salt intake. The salient clinical, laboratory, and pathological findings in cases reported in the literature are reviewed according to the proposed criteria. The authors are of the opinion that salt-losing nephritis is probably a variant of chronic glomerulonephritis or pyelonephritis in which deterioration of tubular function for the reabsorption of sodium chloride has proceeded more rapidly than deterioration of glomerular function. The prostration of the patients and its relief by salt are so dramatic, however, that the term deserves retention as designating a separate clinical entity.

Necrotizing Renal Papillitis: Twenty Cases from Medical Department: Is Incidence of the Disease Increasing? G. T. Pedersen and M. Schwartz. Ugesk. læger 118:829-834 (July 19) 1956 (In Danish) [Copenhagen, Denmark].

In 1953 one case of necrotizing renal papillitis was seen in medical department B of Bispebjerg Hospital; in 1954 there were seven cases; in 1955, 12 cases. The disease had not been encountered the two preceding years. In all but one case the diagnosis was verified at autopsy. The clinical picture did not differ from that observed earlier but was unilateral and marked by progressive uremia. Only three of the patients had diabetes. The causes of the increase are not known.

Necrotizing Renal Papillitis with Partial Reduction of Renal Function. F. Quaade. Ugesk. læger 118:845-846 (July 19) 1956 (In Danish) [Copenhagen, Denmark].

A man aged 43 with post-traumatic stricture of the urethra and history of recurrent urinary infection for 13 years developed marked thirst and polyuria. Diabetes insipidus and psychogenic polydipsia were excluded. Necrotic papillae were excreted the urine. Pyelography with sodium acetizoate diagnosis of necrotizing renal papillitis. E renal function showed a discrepancy between almost normal glomerular filtration and severely damaged tubular resorption. The case is regarded as an extreme example of the type of renal impairment met with in other conditions in which the pathological lesion wholly or mainly involves the distal part of the nephron.

Necrotizing Renal Papillitis: Case Followed More Than Six Years with Histological Verification by Voided Papillae. G. T. Pedersen. Ugesk. læger 118:846-847 (July 19) 1956 (In Danish) [Copenhagen, Denmark].

The author reports a case of papillary necrosis in a woman aged 53 who did not have diabetes mellitus and who at the start of the disease did not present signs of obstruction in the urinary tract. During six years' observation renal papillae were voided regularly. Treatment has been purely symptomatic and the patient has remained able to work in spite of gradually reduced renal function.

SURGERY

Surgical Treatment of Children with Coarctation of the Aorta. A. L. d'Abreu and C. Parsons. Brit. M. J. 2:390-393 (Aug. 18) 1956 [London, England].

During a period of five years at the Children's Hospital, Birmingham, 30 infants died from coarctation of the aorta within six months of birth. During the rest of the first decade a child with coarctation appears to be comparatively safe, but the hazard to life increases again at puberty, and the chances of reaching the age of 40 are poor. Operation has proved easier and safer in children than in adult subjects, and has usually been followed by a fall of blood pressure that has been progressive for a period of several weeks. Stricture formation may follow operative treatment. Subclavian aortic anastomosis, which should be regarded only as a substitute for the better end-to-end anastomosis, had to be used in two patients in whom this occurred. In the first case, after a long and difficult dissection and end-to-end anastomosis, the lower aortic segment developed a linear tear an inch in length. This was repaired, but further severe bleeding from the anastomosis required a rapid suture of both ends. The boy's condition became critical, and the operation was abandoned. Three weeks after this disaster his blood pressure was 240/170 mm. Hg and he complained of intractable headache; the chest was reopened and a large subclavian artery was divided, turned down, and anastomosed end-to-end to the lower aortic segment. Recovery was rapid, and five years later he was well, with a normal blood pressure. In the second case the stenosed area reached so high up to the arch that only an aortic graft or a subclavian aortic anastomosis would have been possible. Grafts were not available at that time, and the subclavian artery was therefore used; the result has been perfect.

Coarctation of the Aorta. W. P. Cleland, T. B. Counhan, J. F. Goodwin, R. E. Steiner. Brit. M. J. 2:379-390 (Aug. 18) 1956 [London, England].

The authors surveyed 52 patients (34 males, 18 females) with coarctation of the aorta treated by them. The patients' ages ranged from one to 55 years. Forty patients, no fewer than 25 of whom were 15 years of age or older, had resections. Of the 12 patients who did not undergo surgical treatment, 6 were over 40 when last seen, but 3 of these have since died, the oldest at the age of 55. Only nine patients presented themselves with symptoms referable to the coarctation; in all the other patients coarctation was found during examinations carried out for other reasons. In all 40 patients subjected to operation the aim was to perform an end-to-end anastomosis to achieve a full aortic lumen at the site of the union. In all cases the coarctation was of the "adult" type. The immediate postoperative course was uneventful in most cases. One patient died six hours after operation from rupture of a suture. Postoperative hemorrhage of severe degree occurred in two cases, but it stopped spontaneously after transfusion. The operation was fatal in three cases. The results have been satisfactory. The brachial blood pressure was lowered toward normal. Postoperative cerebrovascular accidents, bacterial infection, aortic aneurysm, and heart failure neither occurred nor recurred.

The pros and cons of operation may be summarized as follows— In favor: (1) the improbability of surviving past middle age; (2) the insidious or sudden nature of serious or fatal complications, such as aneurysm, endoaortitis, and cerebrovascular accident; (3) the reduction of blood pressure after operation; and (4) the low operative mortality. Against: (1) the difficulty of judging the risks to life in any individual patient; (2) the uncertainty that resection will prevent the onset of serious complications; and (3) the reluctance to subject a symptomless individual to a major operation of a prophylactic nature. Serious consideration of this difficult problem has led the authors to believe that the pros outweigh the cons. Consequently they recommend resection in all patients under the age of 40 unless it is contraindicated by the presence of severe associated cardiovascular anomalies unlikely to be affected by the resection. The ideal time for operation is before adolescence, because then the vessels are healthier and local vascular complications are less common. In addition, the likelihood of obtaining normal postoperative blood pressures is probably greater in the younger individual. Thoracotomy is tolerated better by the young, and anxiety states are unusual at this age. A relatively serious operation of election should be carried out before the individual has acquired responsibilities and dependents.

Carcinoma of Esophagus: Thirty-Three Cases. J. Costas Durieux. Bol. Asoc. méd. Puerto Rico 48:207-212 (May) 1956 (In Spanish) [Santurce, Puerto Rico].

Thirty-three hospitalized patients of both sexes with cancer of the esophagus are reported on. Most of the patients were between the ages of 50 and 70 years. The predominant symptoms were acute dysphagia and rapidly progressive loss of weight. In the majority of the cases the cancer was located in the middle fourth of the esophagus. The diagnosis was made radiologically and by esophagoscopy. Eleven patients were in an inoperable stage because of old age and cachexia. Of the 22 patients who were in an operable stage, only 11 were able to undergo resection. The lesion was located in the upper fourth of the esophagus in one patient, in the lower fourth in six, and in the middle fourth in four cases. Restoration of continuity of the alimentary tract was accomplished by esophagogastrostomy or by the use of a plastic tube. In the group of 11 patients who underwent resection there were four postoperative deaths, due to the following complications: coronary thrombosis, cerebral hemorrhage, renal insufficiency, and adrenocortical insufficiency. Rupture of the anastomosis occurred in no case. Two patients had a complicating fistula that healed spontaneously. One of these patients had a plastic tube for restoration of continuity of the alimentary tract. The author concludes that resection of the segment of esophageal cancer and restoration of continuity of the alimentary tract, either by esophagogastrostomy or with the utilization of a plastic tube, give satisfactory results in cases of resectable cancer of the esophagus. Resectability of cancer of the esophagus is inversely proportional to the height of the segment in which the lesion is located.

Early Clinical Results of Extended Radical Operation for Carcinoma of the Breast: Report on 100 Cases. W. Lentz. Beitr. klin. Chir. 193:64-68 (No. 1) 1956 (In German) [Munich, Germany].

A report is presented on the first 100 patients with carcinoma of the breast who underwent extended radical operation at the surgical clinic of the University of Kiel. The term "extended radical operation" is proposed for the operation, which combines Halstedt's classic radical operation with the resection of the internal mammary lymph node chain (parasternal lymph node chain). In the first operations the second or third costal cartilage was removed only occasionally, while in the operations that were performed later, the second and the third, or the second, third, and fourth costal cartilages were removed, always close to the sternum, about 1.5 to 2 cm. lateral to it, so that the mammary vessels with the lymphatic chain and surrounding adipose tissue could be clearly seen and removed. The operation was performed with the patient under intratracheal anesthesia. Thus it was possible to avoid a postoperative pneumothorax when the pleura was incised, as happened in 17 patients. Although a postoperative pleural effusion was observed in 10 of the 17 patients, and in an additional 9 patients, the pleural cavity did not become infected in any of them. In contrast to the plain radical operation, another typical complication of the extended radical operation consisted of secondary healing of the operative wound in 25 patients, in most of whom an accumulation of fluid had occurred in the area of resection of the costal cartilages. Four of the 100 patients died on the 6th, 15th, 21st, and 35th postoperative days respectively. These four patients were between the ages of 68 and 75; death resulted from embolism in two, from cardiac decompensation in one; and from a tension pneumothorax in one. The death of the last patient was most likely the result of the extended operation. The increased incidence of complications should be kept in mind when a decision must be made concerning the performance of an extended radical operation in a poor-risk patient.

Carcinoma of the Breast Metastasizing in the Mammary Lymph Node Chain: Report on 100 Cases. R. Graf. Beitr. klin. Chir. 193:90-97 (No. 1) 1956 (In German) [Munich, Germany].

Forty-one of the first 100 patients with carcinoma of the mammary gland who underwent extended radical operation at the surgical clinic of the University of Kiel, Germany, were in stage 1 and 59 were in stage 2 according to Steinthal's classification. Patients in stage 3 were not subjected to this type of operation. Parasternal metastases were observed in 5 (12%) of the 41 patients, and in 25 (42%) of the 59 patients. Twenty of the 41 stage 1 tumors were medial or central and 21 were lateral; metastases in the intermammary lymph node chain had developed from 4 of the 20 medial tumors and from only one of the 21 lateral tumors. Twenty-two of 59 stage 2 tumors were medial or central and 37 were lateral; metastases in the intermammary lymph node chain had developed from 13 of the 22 tumors, and from 12 of the 37 tumors. Frequently the metastases in the intermammary lymph node chain could not be recognized on macroscopic examination. It was only on microscopic examination that the following observations were made: Two small cancer nests were found in the marginal sinus of a parasternal lymph node. Cancer cell emboli in smaller or larger amounts frequently caused complete obstruction of the lymph vessels. When this happened, the carcinoma perforated the lymph vessel wall and continued its infiltrating growth in the parasternal adipose tissue. Finally the carcinoma also invaded the intercostal muscles, and occasionally the pleura. These observations show that clean removal of the entire parasternal tissue similar to that of the axillary tissue is required.

Infusion of 10 cc. of India ink into the sternal marrow of 30 cadavers and injections of 2 cc. of Trypan blue into the sternum of two dying patients revealed several lymphatic connections between the left and the right mammary glands. Such connections were observed between the superficial lymphatic network of the left and the right mammary glands in the areas of the cutis and the subcutis, and in addition between the right and the left intermammary lymph node chains retrosternally at the level of the second intercostal space, behind the manubrium in the area of the anterior mediastinum, and also intrasternally through the marrow cavity of the sternum.

Erythromycin Treatment of Staphylococcus Enteritis. E. H. Thaysen, K. H. Eriksen, H. E. Knutsen and F. Neukirch. Ugesk. læger 118:741-746 (June 28) 1956 (In Danish) [Copenhagen, Denmark].

In five out of six grave or moderately grave cases of micrococcic (staphylococcic) enteritis in which the tetracyclines were discontinued and erythromycin treatment instituted, rapid improvement resulted; one patient died, possibly because of too late start of the erythromycin treatment. Six additional cases of micrococcic enteritis not previously published are cited; the three in which the tetracyclines were not discontinued in spite of marked symptoms of micrococcic enteritis were fatal, and two of the three in which the tetracyclines were discontinued shortly before or on the appearance of the enteritis were fatal. The favorable experiences with erythromycin should not lead to its application in every case of diarrhea that may occur during treatment with tetracyclines, as the diarrhea usually ends on discontinuation of the tetracyclines. Grave toxic micrococcic enteritis is a rare complication. Too liberal use of erythromycin may increase the danger of development of resistant Micrococcus strains. Two factors are important in the prognosis in grave micrococcic enteritis: (1) immediate discontinuation of the tetracyclines and (2) oral administration of erythromycin if the diarrhea has not abated essentially during the first 24 hours. If the patient is seriously affected, this time interval may have to be shortened. Micrococcic enteritis is thought to be mainly nosocomial; one of the cases treated with erythromycin originated during Aureomycin treatment in the home and shows the possible risk in ambulant Aureomycin treatment of patients recently discharged from hospital.

Two Fatal Cases of Staphylococcus Enteritis After Antibacterial Treatment. T. Frederiksen. Ugesk. læger 118:739-741 (June 28) 1956 (In Danish) [Copenhagen, Denmark].

Two fatal cases of micrococcic (staphylococcic) enteritis after treatment with broad-spectrum antibiotics were observed within three months. In the first case, with a characteristic picture, the onset on the fourth day after the start of Terramycin treatment points to Terramycin as the cause of the enteritis. Death occurred on the following day. The nausea that appeared in the second case two days after the start of Aureomycin treatment was regarded as one of the ordinary complications following the administration of Aureomycin, but use of the agent was discontinued. Twelve hours later the patient's temperature had risen to 40.3 C and the clinical course was characteristic of micrococcic enteritis. The patient died three and a half days after institution of the Aureomycin treatment. In both cases cultures from the intestine showed growths of micrococcus Pyogenes var. aureus.

A Study of Hürthle-Cell Tumors of the Thyroid Gland: Report of Nine New Cases. D. C. Collins. A. M. A. Arch. Surg. 73:228-240 (Aug.) 1956 [Chicago].

Since 1907, when Langhans presented the first report, a total of 384 instances of Hürthle-cell tumors of the thyroid have been reported by 44 authors. Eleven different theories have been suggested to explain the origin of the Hürthle cell. The cell should really be called the "Baber cell," for it was Baber who first described it in 1877 and 1881. The cell is only a physiopathological variant of thyroid epithelium, representing an involutional or degenerative change. The author investigated Hürthle-cell tumors observed at the Hollywood-Presbyterian Hospital between 1924 and 1955 and presents observations on nine new instances of Hürthle-cell tumors reported for the first time. One tumor was a low-grade, well-encapsulated adenocarcinoma. Another lesion was a recurrence of a Hürthle-cell adenocarcinoma six years after a total thyroidectomy and was a single metastasis to a right cervical lymph node. The remaining seven were benign lesions, one demonstrating a Hürthle-cell reaction widely throughout a Hashimoto struma. Eight of the nine patients at a recent follow-up were alive and free from recurrence. Nine photomicrographs illustrate the characteristic histological appearance presented by each of the nine lesions. Hürthle-cell reactions do occur in various conditions of the thyroid, in a microscopically normal gland, in one with nodular nontoxic adenomas, and in the presence of Hashimoto's struma.

Most of the Hürthle-cell tumors that have been observed in the United States have been benign well-encapsulated adenomas. A more proper term for these tumors would be "eosinophilic large-celled tumor of the thyroid," as recommended by Willis in 1948. In the thyroid carcinomas characterized by a blotting out of the original histological picture by a degenerative eosinophilic change (Hürthle-cell reaction), the final degree of malignancy of the particular tumor will probably depend largely on the character of the original malignancy. It appears that a Hürthle-cell reaction in thyroid tissue indicates both a more favorable prognosis and a diminished growth capacity on the part of the original tumor. Most Hürthle-cell adenocarcinomas of the thyroid gland are rather benign and metastasize late, and then usually only into the neighboring areas of the neck. This behavior is in sharp contrast to that of the tumor originally described by Langhans, in Europe in 1907, which possesses a high degree of malignancy and metastasizes widely early in the course of the disease. Highly malignant lesions are still recorded in the current medical literature from other portions of the world. From the available American case reports collected to date, it seems that a complete lobectomy, including the thyroid isthmus, will usually result in a permanent cure of the Hurthle-cell adenocarcinoma, if it is completely removed at the first attempt. To prolong life and keep the number of recurrences of malignant tumors of the thyroid gland to a minimum, solitary nodules in one lobe of the gland should always be removed by total lobectomy including the isthmus. The practice of either cutting into a solitary adenoma of the thyroid or attempting to remove only that adenoma from a lobe is fraught with danger.

The Use of Radioactive Iodinated Serum Albumin for Blood Volume Determinations.

S. B. Marshall and K. R. McKenzie. Rocky Mountain M. J. 53:704-707 (Aug.) 1956 [Denver].

The use of iodine-131 tagged human serum albumin seems best to fulfill the requirements of speed, consistency, and accuracy. The iodinated albumin is made from salt-free human albumin and can be purchased from laboratories. Approximately 10 mg. of albumin is iodinated with 500 μc of I^{131}, or two moles of iodine to each mole of albumin of 60,000 molecular weight. It is shipped from the laboratory in 1-mc lots and contains less than 1% free iodide. The 1-mc shipment (approximately 1 ml.) of albumin is diluted to 50 ml. with isotonic sodium chloride solution, giving an initial dosage of 20 μc per milliliter. One milliliter of the diluted albumin is diluted to 500 ml. in a volumetric flask for preparation of the standard. For each determination, 0.5 to 1 ml. of the iodinated albumin (5 to 10 μc) is drawn into a calibrated tuberculin syringe and injected into an antecubital vein. The syringe is then routinely "washed out" by withdrawing blood and pushing it back into the vein. Ten to twelve minutes after injection a venipuncture is performed in the opposite antecubital vein and from 8 to 10 ml. of blood is removed in a heparinized syringe. The blood is placed in a labeled centrifuge tube, and may be analyzed immediately or after a period of several hours, since the unknown is compared to a standard having the same decay rate. Exactly 1 ml. of whole blood from the centrifuge tube is carefully pipetted into a small glass counting vial. The remaining blood is centrifuged for five minutes at 3,000 rpm, and 1 ml. of plasma is pipetted into a similar vial. A well-type scintillation counter with an attached decimal scaler is used for measurement of radioactivity. The background count is measured first, and this value is subtracted from all subsequent calculations in order to give specific activity. One milliliter of the previously prepared standard is pipetted into a third similar counting vial. Counts are then made on blood, plasma, and the standard. Blood and plasma volumes are calculated separately according to a formula.

This method was used on a group of 30 nurses, and on 30 male patients free from derangement of blood volume, in order to establish normal values. The results obtained were compared with those recorded in Denver by the Evans Blue method and with volume measurements made at lower altitudes, utilizing both the iodinated albumin and dye methods. Normal values in these four studies are presented in a table. The history of a patient with multiple contusions and a compound skull fracture is presented to show the clinical usefulness of measuring blood and plasma volume in a surgical patient by means of the method described.

Implantation of the Left Internal Mammary Artery in the Myocardium: A Histopathological Evaluation After Six Months.

R. Maniglia and A. A. Bakst. A. M. A. Arch. Surg. 73:187-191 (Aug.) 1956 [Chicago].

Maniglia and Bakst direct attention to Vineberg's experiments on the transplantation of the left internal mammary artery in the heart of dogs, which aimed at increasing the collateral coronary blood flow of the myocardium. Since Vineberg's observations were not extended beyond the 11th week, the authors made observations over a longer period. They opened the chests of nine mongrel dogs through the fifth intercostal space and dissected the left internal mammary artery off the chest wall, from the sixth to the fourth intercostal spaces. The intercostal vessels and the distal segment of the internal mammary artery at the sixth interspace were doubly ligated and transected between ligatures. A tunnel was prepared in the anterior wall of the left ventricle, and the vessel was pulled into it. The sixth intercostal vessel was transected before transplantation so that blood flowed freely from it; then it was buried in the myocardial tunnel.

Six months later the animals were anesthetized, and the chest was opened to perform physiological studies on the coronary blood. The animals were killed immediately after these studies, and the hearts were fixed in a 10% formalin solution. After fixation the myocardial tunnel containing the implanted artery was arbitrarily divided into quarters, and sections including the entire thickness of the myocardium were taken from each. Quantitative measurements of the collateral blood flow at the end of six months failed to reveal an increase in collateral circulation. This is explained on the basis of histological studies of the implanted artery showing consistent narrowing of the lumen by intimal fibroelastosis and occlusion of the lumen by thrombus.

Resection in the Treatment of Pulmonary Tuberculosis in Children and Adolescents: Report on 26 Cases.

M. A. Lassrich and F. Sturtzbecher. Arch. Kinderh. 153:201-224 (No. 3) 1956 (In German) [Stuttgart, Germany].

The authors describe observations on 26 children and adolescents who were subjected to pulmonary resection during the period from 1951 to 1954 in the surgical department of the University Hospital of Hamburg-Eppendorf in Germany. The operations consisted of a wedge excision, segmental resections, lobectomy, or pneumonectomy. The indications for these operations in 12 of the patients were pulmonary cavities that were either unsuitable for collapse therapy or had resisted such treatment. In eight children resection was necessary because of destructive pulmonary processes secondary to bronchiectasis; three children had honeycomb lung with tuberculosis superinfection, and in the three remaining patients resections were carried out because of caseous pneumonia, tuberculoma, or because of a "destroyed lung." These six different types of lesions are further illustrated on the basis of eight case reports outlining the history, roentgenologic findings, indications for resection, type of operation, and histological findings on the surgical specimen.

From 18 months to 4½ years have elapsed since the operations were carried out. All patients received sanatorium care for a period of three months after the pulmonary resection. A serious complication in the form of a bronchial fistula developed in one of the patients but was cured by surgery. All patients experienced a decisive improvement as a result of the pulmonary resection. Excretion of bacilli was arrested immediately. The patients showed improvement in general condition and an increase in weight; some of them were able to resume their occupations. This shows that the immediate results were favorable, however, more time will be necessary to estimate the final results of the pulmonary resections.

Observations on Cardiospasm and Its Treatment by Brusque Dilatation.

R. Schindler. Ann. Int. Med. 45:207-215 (Aug.) 1956 [Lancaster, Pa.].

Eighty-four patients with cardiospasm associated with distressing dysphagia were treated by brusque dilatation with the Starck metal dilator. The patient is told that the dilatation is a major operation, even though it lasts only a few seconds. The diagnosis, made usually from the typical case history and the roentgen pictures, should never be taken for granted. Obstruction by carcinoma or by scar must be excluded. The best method for establishing the diagnosis is the introduction of a thick no. 44 F. bougie. This will usually stand on the obstacle for a few seconds or minutes and will suddenly "drop" into the stomach. For the dilatation the patient is hospitalized and receives penicillin and streptomycin, and his stomach and esophagus are carefully lavaged. He should not receive sedatives, which might relax his muscles and prevent their desirable forceful rupture. After the usual local anesthesia of the throat, the dilator is introduced into the stomach and the position of its dilating portion exactly at the point of narrowing is verified fluoroscopically. At this moment the patient is told that he will feel an atrocious pain but that under no condition must he move. Then, when the patient is as tense as possible, the instrument is opened forcefully, often against a marked resistance. The operator's hand often seems to feel hard tissue broken up. If that happens, success can be predicted, although sometimes cures are obtained if this frightening sensation is not experienced. Eighty (95%) of the 84 patients were cured, and 4 (5%) were therapeutic failures. Complications occurred in five patients, three of whom had fever readily treated by antibiotics and two of whom had small lesions of the stomach. The cure of cardiospasm by brusque dilatation is usually permanent.

Two different types of cardiospasm were detected in these patients. In 81 patients the typical point of obstruction was the lowermost segment of the esophagus, extending from a few centimeters above the diaphragm to the cardia. It has been assumed that the closed segment of the esophagus constitutes a physiological entity, the "vestibulum," the border of which toward the esophagus proper contains a true sphincter muscle. This vestibulum opens only at the end of the act of swallowing, and the true picture of cardiospasm is composed of faulty, irregular innervation of the esophagus and inability of the vestibulum to open properly. The enormous resistance often felt during the act of dilatation can be caused only by a powerful muscular or tendinous organ, i. e., the diaphragm. That does not prove that the diaphragm itself is the obstructing structure. It may be that its tearing is only a by-product of the procedure and that the cure is effected by the dilatation of the vestibulum. It is probable that the essential faulty innervation remains unchanged and that the esophagus empties only by gravity. The roentgenologic appearance of the esophagus, however, often changes, so that, as far as its diameter is concerned, it resembles a normal one. Only three patients had the rare second type of cardiospasm in which the point of obstruction seemed to lie in the cardia itself. In one of these three patients no cure was obtained by brusque dilatation. There was no evidence in any of the 84 patients that cardiospasm is a purely psychogenic disease.

Effects of Pedicled Grafts of Jejunum in the Wall of the Stomach: Long Term Follow-Up Study. S. W. Moore. Ann. Surg. 144:152-158 (Aug.) 1956 [Philadelphia].

A long-term follow-up of 11 patients in whom a jejunal pedicled graft was implanted in the wall of the stomach showed no significant change in the gastric acidity as measured by the free hydrochloric acid. In 3 of the 11 patients ulcers developed in the jejunal pedicled graft. Nine of the 11 patients had poor results. Five of the nine patients with poor results had excellent results after a subtotal gastric resection.

The Hepatorenal Syndrome: A Historical Review. E. Cardi. A. M. A. Arch. Surg. 73:224-227 (Aug. 1956) [Chicago].

Cardi says that before 1913, when Marklen first used the term hepatorenal syndrome, the condition was referred to as the renal complication of obstructive jaundice. Other terms applied to this syndrome were urohepatic syndrome, hepatourologic syndrome, hepatic death, cholemic nephrosis, and bile nephrosis. Cardi discusses the historical development of the concept of the hepatorenal syndrome and of acute tubular nephrosis with special emphasis on the clinical and pathological manifestations. He reviews the extensive literature dealing with experimental studies on this syndrome and discusses the various disease states associated with it. The vascular peculiarities of the liver and kidneys are described to give a better insight into the pathogenesis of the syndrome. The review of the historical, clinical, and experimental literature leads to the conclusion that the hepatorenal syndrome is simply an acute tubular nephrosis precipitated by hepatic insufficiency.

Polyposis of the Colon. C. T. Flotte, F. C. O'Dell Jr. and F. A. Coller. Ann. Surg. 144:165-169 (Aug.) 1956 [Philadelphia].

Polyposis is a rare familial disease in which hundreds of polyps develop in the colon and rectum, usually about the time of puberty. There is a marked tendency for these polyps to undergo malignant degeneration while the patient is still relatively young. Of 63 patients with polyposis of the colon observed at the University of Michigan Hospital in the past 20 years, 40 were treated with either total or subtotal colectomy. The average age of the patient at the time the disease was diagnosed was 33.7 years. Twenty patients (50%) were found to have carcinoma of the colon at operation. Carcinoma subsequently developed in the rectal segment of four patients subjected to subtotal colectomy. Care must be taken to select for subtotal colectomy those patients who will cooperate by returning for periodic sigmoidoscopy and removal of recurrent polyps. Nineteen patients are alive and well without evidence of malignancy. Polyposis is originally a benign, although precancerous, disease, but the finding of carcinoma when the diagnosis of polyposis is first established is so common that it should always be considered as a malignant disease and treated accordingly.

Surgical Therapy in the Treatment of Diverticulosis and Diverticulitis of the Colon. M. N. Malinowski, J. E. Lutz and K. G. MacDonald. West Virginia M. J. 52:289-292 (Sept.) 1956 [Charleston].

An analysis of 66 patients admitted to the Memorial Hospital of Charleston, W. Va., between April, 1952, and October, 1955, for diverticulosis and diverticulitis is presented. The group included 36 women and 30 men, and the ages of the patients ranged from 41 to 81 years. Generally, there are three stages in the development of this pathological state, namely, the prediverticular stage characterized roentgenologically by loss of colon segmentation, the stage of formed outpouchings or diverticula (diverticulosis), and the stage of an infected diverticulum, termed diverticulitis. Of the 66 patients reviewed 39 had diverticulosis without or with only very mild symptoms. Twenty-nine patients had acute diverticulitis that responded to medical treatment. Seven patients, five of whom were women, required surgical treatment. Diverticulitis, like peptic ulcer, is treated primarily by the internist. Most patients can be managed by rest, diet, antispasmodics, and antibiotics. Surgery is required chiefly for complications, which occur in up to 20% of the patients.

The surgical treatment must be fitted to the individual patient and the type of lesion encountered. Drainage of localized peritonitis with transverse colostomy often will prove a life-saving procedure and will facilitate a fairly simple resection later on. Conservative treatment in spite of repeated, acute attacks may lead to difficult complications. Since 1950, prophylactic resection during a quiescent period has been shown to have much to recommend it and has been accomplished with little risk. This should be considered in patients in whom a persistent mass is found, and recurrent obstruction, recurrent hemorrhage, marked urinary symptoms, or malignant changes cannot be ruled out. In older persons the authors always suggest a preliminary transverse colostomy even though it requires three procedures instead of one and is more costly. In the case of obstruction of the colon secondary to diverticulitis, especially where there is a disparity in size between the proximal and the distal colon a transverse colostomy should be done.

Mesenteric Vascular Occlusion. G. S. M. Wilson and J. Block. A. M. A. Arch. Surg. 73:330-345 (Aug.) 1956 [Chicago].

Mesenteric vascular occlusion is not so rare as is generally believed. Thirty-two cases were observed in a Manchester hospital during the period January, 1948, to June, 1951. Fourteen occurred in patients under treatment in the medical wards for some other condition, and the remaining 18 patients were either treated in the surgical wards or else were seen by a member of the surgical staff in consultation. Hemorrhagic infarction has been emphasized to such an extent that most surgeons regard it as the only pathological evidence of acute mesenteric vascular occlusion. A few authors have described a type of so-called "anemic infarction," which is rare and was not observed in the cases reviewed here. The authors draw attention to another manifestation of occlusion of the superior mesenteric artery observed at operation in some of their patients. These changes were only fully appreciated in the third patient in whom they occurred. The intestine was pale, with a bluish tinge in parts, and was contracting vigorously. Blood in the lumen was visible through the wall of the intestine, and there was little if any peritoneal exudate. The mesentery itself showed no edema or hemorrhages, but it was noted that the arteries supplying the affected intestine were not pulsating. This was seen in the vasa recta adjacent to the intestinal wall, and a sudden transition to normally pulsating vessels was noted at either end of the affected segment. In another patient a correct diagnosis of mesenteric embolism was made but rejected at operation because the intestine looked "normal." This was because it was contracting actively and the mesenteric vessels were not examined closely enough in the absence of signs of hemorrhagic infarction. After autopsy had confirmed the diagnosis, it was recalled that the intestine had looked pale. The authors feel that it was only because of this unfortunate experience that the third patient was accurately assessed at operation.

They comment on venous and on combined arterial and venous occlusion and on associated pathological conditions, such as heart disease, pulmonary infarction, and multiple emboli. During the past 20 years, a number of articles have been published in continental and Latin American journals describing cases of intestinal infarction not due to organic vascular occlusion and reversible in the early stages. Various explanations have been offered—anaphylaxis, arterial spasm, and impaired capillary permeability. Divergent methods of treatment, such as the injection of epinephrine and procaine sympathetic block, have been advocated. British and North American literature is silent on the subject, but one of the authors (Block) has seen several cases of anaphylactic shock, associated with severe abdominal pain, dramatically relieved by epinephrine. All the patients in the series described eventually died. Of the 32 patients only 12 were subjected to operation, and, of these, 2 may be deemed to have technically survived the procedure. Most of the patients showed extensive infarction and serious associated lesions. In at least 75% of arterial occlusions the main stem of the superior mesenteric artery was occluded above the ileocolic branch.

NEUROLOGY & PSYCHIATRY

Cases of Atypical Poliomyelitis. C. Hooft, A. Vermassen and M. J. Delbeke. Maandschr. kindergeneesk. 24:185-192 (June) 1956 (In Dutch) [Leyden, Netherlands].

In the course of seven months a total of 178 children were referred to the authors with a diagnosis of probable poliomyelitis. In 20 of these children this diagnosis could be ruled out on the basis of clinical examination and of the results of spinal puncture and of virological examinations. One hundred-fifty of the remaining 158 patients had the classic forms of poliomyelitis; 7 had the meningeal form, 102 had the spinal form, and 41 had respiratory, bulbar, or encephalitic forms. Complete virological and serologic tests revealed the type-1 poliomyelitis virus in 94% of these patients. The authors report histories of eight children with atypical forms of poliomyelitis in whom virological examinations of the feces or antibody determinations demonstrated the viral nature of the infection. The eight children included four with temporary palsies of short duration, one with spastic tetraplegia, one with focal encephalitis without sequels, one with temporary, acute cerebellar ataxia, and one in whom poliomyelitis was complicated by meningococcic meningitis.

Poliomyelitis in Pregnancy: Effect on Fetus and Newborn Infant. M. Siegel and M. Greenberg. J. Pediat. 49:280-288 (Sept.) 1956 [St. Louis].

A prospective study was made of the outcome of gestation after the occurrence of poliomyelitis in New York City between 1949 and 1953, inclusive. During this five-year period, 87 cases of poliomyelitis were observed in pregnant women. Twenty-three of the women had the nonparalytic type of the disease, and 64 had paralytic types of the disease. The 87 pregnancies complicated by poliomyelitis resulted in 86 single births and one set of twins. There was no evidence of an increase in congenital defects and inconclusive evidence of an increase in prematurity among the 88 products of gestation. Seven (35%) of the 19 fetal deaths were observed in pregnancies complicated by the onset of paralytic poliomyelitis in the first trimester of gestation, and 14 (46.7%) fetal deaths were observed in pregnancies complicated by the onset of poliomyelitis of all clinical types in this trimester. Most of these dead fetuses were delivered within two weeks after the onset of clinical infection, and the fetal deaths appeared to be directly related to the occurrence of poliomyelitis in the mother. The incidence of fetal deaths decreased markedly with the onset of poliomyelitis in the second and third trimester of gestation.

Three cases of paralytic poliomyelitis occurred among the 69 live births. All three infants were delivered within 24 to 48 hours of the onset of neurological signs of poliomyelitis in the mother. Symptoms of paralysis in the newborn infant were observed within from 6 to 10 days after delivery. Neonatal poliomyelitis thus occurred only in infants whose mothers had poliomyelitis near term and who were born shortly after the onset of the disease in their mothers. This group is presumably unprotected by maternal antibodies and may be heavily exposed to maternal infection in the uterus, during delivery, and after birth. An increase in the neonatal mortality rate was noted that was related to neonatal poliomyelitis and to anoxemia after postmortem cesarean section in women dying of bulbar poliomyelitis.

Poliomyelitis in the Netherlands During 1955: Results of Virologic and Diagnostic Investigations. B. Hofman, A. Kret, H. A. E. van Tongeren and J. D. Verlinde. Nederl. tijdschr. geneesk. 100:2038-2045 (July 21) 1956 (In Dutch) [Haarlem, Netherlands].

Four hundred sixty-nine cases of poliomyelitis were officially reported in the Netherlands during 1955. Of 126 virus strains isolated, 37% were type 1, 57% type 2, and 6% type 3. The type-2 strain of poliomyelitis virus predominated from July to September and type 1 from October, 1955, to January, 1956. In the eastern provinces of Gelderland and Overijsel, poliomyelitis began in May and reached its peak in September, and the majority of strains isolated in those provinces belonged to type 2. In the western and southern provinces of South-Holland and North-Brabant, particularly in the region of Rotterdam and Dordrecht, poliomyelitis started in June and reached its greatest incidence in October. The greatest majority of poliomyelitis virus strains isolated in this region were of type 1. Virological studies were made in 498 patients. The percentage of isolations of poliomyelitis virus were highest (67) in the patients with paralytic poliomyelitis; for the meningeal and abortive forms of poliomyelitis the percentages of virus isolations were 17 and 12 respectively. Mixed infections of poliomyelitis with Coxsackie virus were observed in 16 patients (3.2%). Infections with group B Coxsackie virus were frequent until October, after which they decreased simultaneously with a sharp increase of type-1 poliomyelitis virus infections.

Incidence of Contact Infection in Poliomyelitis (Institutional Epidemic). H. Lennartz and B. Rohde. Monatsschr. Kinderh. 104:311-314 (July) 1956 (In German) [Berlin, Germany].

An epidemic of poliomyelitis occurred in a home housing 66 children and their nursing personnel near Bremen, Germany, in September, 1953. The children ranged in age from 3 months to 6 years. There was little contact between the residents of the home and the surrounding population, and no cases of poliomyelitis had been observed in the surroundings before the institutional outbreak. Paralytic poliomyelitis developed in 14 of the 66 children, and in one of the 14 an ascending paralysis caused death. The proportion of children who contracted poliomyelitis was about the same as that observed in other institutional outbreaks (about 20%). It was noteworthy that no purely meningeal forms of poliomyelitis occurred and that with the exception of the fatal case only the lower extremities were involved. The percentage of children with residual paralysis in the lower extremities was unusually high, that is, 12 of 13 showed such residual lesions. The authors believe that intramuscular injections during the incubation period were responsible for this. Outbreaks of whooping cough and varicella in the course of which intragluteal injections of penicillin and other drugs had been given had preceded the poliomyelitis epidemic. Moreover, five days after the appearance of the first case of paralytic poliomyelitis the children had received intragluteal injections of gamma globulin.

The fact that this epidemic of poliomyelitis occurred in children who had been isolated in an institution since birth induced the authors to investigate questions concerning the virus and its occurrence in the blood and feces of children with symptoms of poliomyelitis and in the contacts. They found that the Brunhilde type of virus was responsible for the outbreak. Virus was excreted in the feces by all but one of the children with active disease and by 80% of the apparently healthy contact children 14 days after paralytic poliomyelitis had developed in the first child, whereas virus was isolated in only two of the nursing personnel. One of these two adults was the cook, whose own child was one of the first in whom poliomyelitis developed, and the other was a 16-year-old nurses' aid. Since viremia can be expected only in the first days of infection, it is understandable that when blood was withdrawn on the 13th day after the appearance of the first case of poliomyelitis there was little promise of success. Isolation of the virus was successful in only one of 52 blood or serum specimens. The positive specimen was from a child without signs of active disease who was excreting virus in the feces but who did not as yet have antibodies against poliomyelitis. At the end of the second period of incubation the majority of children not only excreted virus in the feces but also had neutralizing antibodies in the serum. After three more weeks had elapsed, that is, at the time of the second blood withdrawal, all children showed the presence of antibodies in the neutralization test. Many showed an increase in antibodies, and the titers were rather high, although these young children had shown no symptoms of poliomyelitis. When, however, the complement-fixation reaction was carried out during the same period, poliomyelitis antibodies were not so regularly demonstrated and an increase was detected only very occasionally.

Brain Lesion After Burns. U. Huschke. Monatsschr. Kinderh. 104:300-307 (July) 1956 (In German) [Berlin, Germany].

Huschke describes observations on the brains of four children and one adult who died as the result of scalds or burns. Three of the four children died within 24 hours and one died seven days after the burn. The adult died two and one-half hours after he had fallen into boiling liquid. The ganglion cells of the brain showed all stages of acute and severe damage, which in some had progressed to complete dissolution. The Purkinje cells were in the most favorable state of preservation. The neuroglia showed mostly regressive changes, without a noticeable increase in gliacytes. Vascular changes consisted chiefly of extreme dilatation, engorgement of the veins, edematous suffusion of the vascular walls, moderate swelling and increase of the capillary endothelium, and severe dilatation of the perivascular spaces, some of them containing homogenous extravasations. The brain volume was greatly increased in all five patients (cerebral edema in three and swelling of the brain in two). This increase in volume involved the entire brain.

Disturbances in permeability with subsequent serous effusion into the cerebral tissues and new formation of intercellular glial fibers are the outstanding changes. The fibrous gliosis progresses as the interval after the burn lengthens and seems to be one of the first manifestations of brain lesions resulting from scalds and burns. The author comments on the possibility of late brain lesions, the result of which may persist after the burn has healed. It seems probable that permanent organic brain damage may progress to atrophy just as do brain lesions of other origins that are associated with acute parenchymal lesions and serous effusion into brain tissues. The clinical effects as regards mental development may be severe enough to result in idiocy.

Diagnosis and Differential Diagnosis of Wilson's Disease (Hepatolenticular Degeneration): On the Basis of Studies on Members of a Family. V. H. Gastager and W. Spiel. Monatsschr. Kinderh. 104:314-318 (July) 1956 (In German) [Berlin, Germany].

Gastager and Spiel report studies on a family with nine children. The parents showed no symptoms of hepatolenticular degeneration (Wilson's disease). The first member of the family seen by the author, in September, 1950, was a 14-year-old girl. In this patient hepatolenticular degeneration was not recognized. Psychiatric symptoms first led to a diagnosis of schizophrenia; later, neurological symptoms led to a diagnosis of a postencephalitic syndrome. A correct diagnosis was made still later in connection with the other cases in the same family. In the second patient, a younger brother of the girl, the psychiatric symptoms again led at first to a diagnosis of schizophrenia, but later, detailed neurological examinations and particularly metabolic studies permitted the correct diagnosis of hepatolenticular degeneration (Wilson's disease) to be made. A third child of the family, a boy, had died in 1937, at the age of 9 years, with symptoms of jaundice, ascites, and tumor of the spleen. According to the father, the terminal symptoms had been similar to those in the other two children. Although autopsy had not been performed in this patient, catamnestic data suggest that this too was a case of Wilson's hepatolenticular degeneration, in which the signs of congestive splenomegaly (Banti's disease) predominated. Examination of the healthy members of the family led to the discovery of one subclinical case of Wilson's hepatolenticular degeneration; in all the others, the metabolic tests were normal. The patient with the subclinical form of hepatolenticular degeneration was the youngest child of the family, who at the time of his examination was 12 years old. He was as yet free from neurological symptoms, but the liver was firm and the spleen showed signs of hardening. Moreover, the copper content of the serum indicated the presence of a subclinical form of Wilson's hepatolenticular degeneration. The studies on the members of this family revealed that Wilson's hepatolenticular degeneration generally appears in three distinct forms. The symptoms are either predominantly psychiatric, neurological, or internistic. The diagnosis of Wilson's hepatolenticular degeneration is often difficult because the psychiatric and neurological symptoms may be absent or are not typical and the Kayser-Fleischer ring of greenish pigmentation on the cornea may be absent. At autopsy the disease may be recognized by the presence of hepatic cirrhosis and by degenerative changes in the basal ganglions. The examination of the serum for a copper-containing protein is the most helpful of the laboratory aids, because in patients with hepatolenticular degeneration this protein body, which because of its blue coloration is known as ceruloplasmin, is practically absent. One of the present authors in collaboration with others has been able to detect subclinical cases in families of patients with hepatolenticular degeneration with the aid of tests that disclose a lack of ceruloplasmin.

Cerebral Palsy: Clinical Survey of 543 Cases. P. Plum. Danish M. Bull. 3:99-108 (July) 1956 (In English) [Copenhagen, Denmark].

From 1948 to May, 1956, the author examined 543 patients with cerebral palsy in the University Pediatric Clinic of the Rikshospital and treated most of them. There were more cases of quadriplegia than usual in the total material because the clinic admits a relatively large proportion of the most severely affected patients. Familial incidence and heredity do not seem to play any numerically significant part in cerebral palsy. The incidence of organic nervous disease in the group with ataxia is twice that in the other groups, which is thought to agree with the conception that ataxia is due to a hereditary trait. Pathological conditions during pregnancy are on the whole hardly of great etiological significance in the development of the disease. Toxemia of pregnancy and hemorrhage probably are exceptions and have a certain etiological significance. The age of the mother seems to be of little importance. Low birth weight is more frequent than normal in all cerebral palsy groups. Complicated deliveries occur more often than normally, particularly in the groups with hemiplegia, quadriplegia, and athetosis. Asphyxia is seen especially in patients with hemiplegia, quadriplegia, and ataxia, and symptoms during the first days of life are most common in those with quadriplegia and athetosis. Severe and prolonged icterus occurs almost exclusively in patients with athetosis. Seizures and spasms are twice as frequent in those with hemiplegia and quadriplegia as in other groups. Impairment of hearing occurs chiefly in patients with athetosis. Mental deficiency is most often met with in those with quadriplegia. In the single groups mental deficiency is higher in patients with convulsions, small head circumference, and strabismus.

PEDIATRICS

Familial Agammaglobulinaemia. R. H. Elphinstone, I. G. Wickes, and A. B. Anderson. Brit. M. J. 2:336-338 (Aug. 11) 1956 [London, England].

The authors describe two brothers with familial agammaglobulinemia. The occurrence of tuberculosis in the older brother and the behavior of the Mantoux reaction is of interest. The disease, which developed after the symptoms of agammaglobulinemia were established, ran its normal course, complicated by septic infections, and was cut short by the usual chemotherapy and antibiotic treatment. The boy's Mantoux reaction remained positive. The younger boy's case of agammaglobulinemia was discovered very early in the evolution of the disease. His serum still contained a very little gammaglobulin. He was first vaccinated with BCG before there were any symptoms suggestive of agammaglobulinemia and the Mantoux reaction became transiently positive. On revaccination the Mantoux became positive, and it has remained so for eight months. The axillary lymph nodes became enlarged, a normal consequence of BCG inoculation. The serum of all available members of the family has been examined by the zinc turbidity test or by electrophoresis. No further case of agammaglobulinemia has been found. Complete genotyping was performed, but no constant feature was discovered that could be related to the appearance of agammaglobulinemia in the two brothers. The significance of the finding of a low erythrocyte sedimentation rate requires further investigation.

Two Cases of Neuroblastoma. V. Migliori. Clin. pediat. 38:173-178 (March) 1956 (In Italian) [Bologna, Italy].

The author defines neuroblastoma as a malignant tumor of the sympathetic system with no chromogen or hormonal characteristics. It originates in the sympathetic system and may affect any area where elements of the sympathetic system tissues are found, e. g., the neck, the thorax, and the abdomen. The abdomen seems to be affected more often than other regions. Neuroblastomas tend to metastasize rapidly. They affect infants more often than adults. The tumor is made up of polymorphous cells, some of which are small and round, with little protoplasm, and with a compact nucleus rich in chromatin. The author describes two cases of neuroblastoma, one mediastinal and one abdominal. The first patient, a 9-year-old child, had severe pain in the right side of the chest; after some time changes in physiognomy appeared. The child did not have fever. Small movable lymph nodes could be palpated in the supraclavicular region. The circulatory and digestive systems were not affected. The spleen and the liver were normal. Histological examination established the diagnosis of neuroblastoma. The child was operated on, and his condition improved for a while, but then it became worse.

The second patient, a child 2 years and 8 months old, had irregular fever, shifting pains in the limbs, general indisposition, and loss of weight. Radiological examination showed a picture similar to that found in osteomyelitis, but the clinical symptoms were different. Histological examination revealed a metastatic neuroblastoma. The skull increased in volume and became irregular in shape after a short time. Bilateral exophthalmos became noticeable. A large tumor, partially calcified, was discovered in the region of the left kidney. The critical condition of the child did not permit urographic examination. The child died four months after the appearance of the condition. The author points out the necessity of early diagnosis and early surgical intervention.

Congenital Methemoglobinemia in the Newborn Period. M. S. Dine. A. M. A. J. Dis. Child. 92:15-19 (July) 1956 [Chicago].

The two cases presented are the first recorded cases of congenital methemoglobinemia diagnosed and treated in the neonatal period. They demonstrate the importance of early diagnosis for the prevention of hypoxia and death. A lavender blue cyanosis is the most marked clinical feature of this disease, in which from 20 to 40% of the hemoglobin is in the methemoglobin form, whereas the normal values are from 0.01 to 1.8%. The enzyme system that regulates the balance between hemoglobin containing iron in the ferrous state and methemoglobin containing iron in the ferric state is disturbed. The administration of reducing substances, such as methylene blue or ascorbic acid, decreases the amount of methemoglobin. Hence this feature is of value in differentiating between congenital methemoglobinemia and cyanotic congenital heart disease.

The two cases described occurred in siblings, of whom the first was treated on the 18th day of life and the second by the fourth hour of life. The diagnosis of congenital or idiopathic methemoglobinemia was established in these two children first by the identification of the typical spectral band of methemoglobin. This band disappeared immediately after the addition of two or three drops of potassium cyanide, and was thus distinguishable from the spectral band of sulfhemoglobin, which remains fixed after the addition of potassium cyanide. Secondly, the abnormally high blood methemoglobin level was reduced by both intravenously given methylene blue and orally given ascorbic acid. Thirdly, there was no history of exposure to substances capable of causing methemoglobinemia, such as contaminated well water, aniline dye in diapers, phenytoin, or coal tar. The clinical course of each infant was typical, as indicated by the fact that methemoglobinemia has persisted, though modified in degree by ascorbic acid and methylene blue. The parents and two older siblings of the patients had normal methemoglobin values. No previous instance of congenital or idiopathic cyanosis was found in the family history. Jaundice appeared in both infants, but the connection, if any, between this condition and methemoglobinemia is not known. The first child has shown marked motor retardation, probably as a result of hypoxia rather than hyperbilirubinemia; the second child has been normal in growth and development, despite severe hyperbilirubinemia requiring three exchange transfusions.

Early diagnosis of this metabolic defect is important, not only to differentiate this disease from congenital heart disease and other causes of cyanosis, but also to prevent the hypoxia that may lead to death or mental and motor retardation.

Epidemic Staphylococcal Gastroenteritis in a Newborn Nursery. R. T. Smith. A. M. A. J. Dis. Child. 92:45-56 (July) 1956 [Chicago].

The micro-organism responsible for most of the infections that occur in the newborn period is the Staphylococcus. The more serious clinical forms of staphylococcic disease usually occur during epidemic outbreaks. Serious forms of staphylococcic infection reported to have occurred during such epidemics include pneumonia, with empyema, and pyopneumothorax and generalized sepsis. The outstanding clinical characteristic of a recent outbreak of neonatal staphylococcic infection in the newborn nursery of the University of Minnesota Hospitals was an unusually severe form of gastroenteritis manifested in some of the infants. Only one previous report deals with gastroenteritis as a primary manifestation of epidemic staphylococcic infection in the newborn infant. The illness began abruptly with severe retching and vomiting in the four infants most seriously affected; in each instance, diarrhea appeared later. Each infant was found to have diminished or absent peristaltic sounds, lack of abdominal distention, and absence of normal intestinal gas patterns in roentgenograms of the abdomen. The clinical course of the four infants was also marked by the development of rapidly spreading skin lesions and epidermolysis and an unusually severe form of tetany. Mild diarrhea developed in eight other infants, and two had skin lesions.

Culture and demonstration of the Staphylococcus on gram-stained smear from stool specimens, as well as its isolation from cultures of the involved skin and nasopharynx, strongly suggested a primary infection by this micro-organism as the cause of the outbreak. The attack rate in this epidemic, which affected 12 of the 21 infants in the nursery and led to the death of one, was about 60%, and the incubation period was probably from two to four days. The source of the infection could not be definitely identified, but circumstantial evidence pointed to exposure during the first few hours of life. Early recognition of staphylococcic infection in a nursery for newborn infants is vitally important if outbreaks of epidemic proportion are to be avoided and treatment is to be properly directed.

Pulmonary Coccidioidomycosis in a Twenty-One-Day-Old Infant: Report of a Case and Review of the Literature. J. R. Christian, S. G. Sarre, J. H. Peers and others. A. M. A. J. Dis. Child. 92:66-74 (July) 1956 [Chicago].

A review and analysis of 99 reported cases of coccidioidomycosis in children is presented. Of these cases 14 were in infants, the majority of them from California. A high proportion occurred in Negroes and Mexicans, but there was no definite correlation of race and mortality. More cases occurred among boys than among girls in the preschool age group. Osteomyelitis is the commonest of a wide variety of reported clinical pictures; among the others were residual pulmonary cavity, valley fever, pneumonia, primary tuberculosis, and meningitis. The average mortality is 33%; it is higher in infants and decreases with increasing age. The diagnosis was made by direct methods, depending on demonstration of the organism (biopsy, smear, autopsy culture, inoculation) or by indirect methods (serological studies, skin tests), or both together. The duration of the disease varied from less than one month to more than one year. No truly curative treatment is known; methods tried included bed rest, general symptomatic and supportive treatment, various medicaments, deep x-ray therapy, and surgical intervention. Six of the 14 infants are known to have died.

Fatal coccidioidomycosis of eight days' duration also occurred in a three-week-old infant in Chicago. The disease was diagnosed at autopsy and the positive findings were limited to multiple nodules in the lungs. The case is unusual for these reasons: the age of the patient; the apparent contraction of the disease in Chicago, far from an endemic area; and the unusual pathological findings, this being the first reported fatal case in a child with miliary pulmonary and lymphatic lesions exclusively. The child's mother had had a coccidioidomycotic granuloma of the right calcaneus from which specific causative organisms were microscopically demonstrated. An operation was performed on her right foot in 1954 in Mexico, and the lesion now appears to be well healed, clinically and roentgenologically. It seems that the mother's lesion was the most likely source of the infection in her child.

Pheochromocytoma in an Eight-Year-Old Boy. W. van Zeben and F. J. van Sprang. Maandschr. Kindergeneesk. 24:215-225 (July) 1956 (In Dutch) [Leyden, Netherlands].

An 8-year-old boy was hospitalized in November, 1955, with a complaint of severe headaches since July, 1955. He had lost weight and was nervous during the day and restless at night. He had repeated attacks of abdominal pain, which were of the piercing type and were localized in the right upper abdomen. These attacks were followed by a headache of right frontal or occipital localization and were accompanied by anxiety, restlessness, and profuse sweating. Blood pressure reached 240/180 mm. Hg, and the pulse rate was as high as 150 per minute. The presence of pheochromocytoma was considered likely, and this diagnosis was verified with the aid of tests with Regitine (phentolamine) and piperoxan.

Preoperative localization of the tumor proved impossible, since presacral air insufflation and intravenous pyelography failed to reveal a clear outline of the adrenals. A median laparotomy revealed a tumor above the right kidney, which was then removed in the course of a thoracolaparotomy. Two months after the operation the patient was free from complaints. An unusual aspect of this case was a strongly positive Rumpel-Leede sign. There is no other report in the literature of the concurrence of this sign with pheochromocytoma.

Precocious Tetany with Periostosis and Recurring Hypocalcemia. R. Debré, P. Mozziconacci, G. Schapira and others. Arch. franç. pédiat. 13:461-476 (No. 5) 1956 (In French) [Paris, France].

The authors report a case of precocious tetany with bony lesions and recurrent hypocalcemia in an infant girl. At the age of 6 days she presented convulsive tetany of extreme intensity accompanied by hypocalcemia varying from 0.45 gm. to 0.50 gm. per 1,000 cc. This tetany was accompanied by bony lesions characterized essentially by a periosteal thickening producing the appearance of a double contour at the diaphysis of the long bones. The tetany responded to treatment with calcium, which resulted in disappearance of the crises, normalization of the blood calcium level, and improvement of the pathological bone pictures. But after one year of development, when the infant had received notable doses of calcium and vitamin D, a lowering of the blood calcium level accompanied by convulsive crises occurred again. Three months later there was another transitory hypocalcemia.

Precocious tetany with periostosis deserves a place among the causes of infantile hypocalcemic convulsions. It starts in the first months of life and progresses toward a recurrent hypocalcemia in spite of the administration of calcium and of vitamin D. This tetany is distinguished from rachitic tetany by the radiological appearance of the osseous lesions. It is also distinct from neonatal tetany, which is always transitory. It is not related to a disturbance in the absorption of calcium but is probably caused by a parathyroid insufficiency rather than a fault in the response of the renal tubule to the parathyroid hormone. It is not necessarily accompanied by the morphological disorders or the intellectual retardation described in certain varieties of chronic idiopathic tetany and in the pseudohypoparathyroidism of Albright.

Indications for Corticotherapy in the Treatment of Tuberculosis in the Child. A. Breton and B. Gaudier. Pédiatrie 11:523-530 (No. 5) 1956 (In French) [Lyon, France].

Two criteria are essential in judging the efficacy of the hormonal treatment of initial tuberculosis: (1) pulmonary x-ray films frequently repeated reveal lesional improvement; and (2) attentive surveillance of the general state shows that all treated children benefit on all the planes of the mode of cure. One notes a regression of functional signs, a rapid normalization of temperature, a certain euphoric state with a revival of appetite, and, very often, a clear rise in the weight curve, which was level or declining at the beginning of the primary infection (gains of 1 kg. per month are frequent in the course of the cure and after its cessation). These pleasing results in the general state and the indisputable regression of the lesions themselves authorize the use of corticotherapy in the treatment of tuberculosis in children. Short cures, always in association with specific antibiotics, provide protection against complications, which are rarely severe. The action of the corticoadrenal hormones as an adjuvant to antibacillary treatment will be better understood and better utilized after more experience. The tuberculous child benefits from this new method of treatment as does the adult. Four clinical forms constitute the essential indications: acute disseminated tuberculosis, recent infiltrating lesions, pleural effusions, and ventilatory disturbances engendered by endobronchitis. Among these indications serous miliary tuberculosis, certain forms of bacillary meningitis, and serous effusions are unanimously recognized. In all other eventualities and in particular during the development of the most common forms of primary tuberculosis, certain improvements can be obtained that should encourage the use of this recent and promising therapeutic agent. The advent of new antibacillary antibiotics, such as cycloserine, does not modify the authors' present therapeutic position concerning hormone therapy in any way.

Investigation of the Efficacy of Pancreatic Substitution Therapy in Cystic Fibrosis of Pancreas. W. K. Dicke. Maandschr. kindergeneesk. 24:226-233 (July) 1956 (In Dutch) [Leyden, Netherlands].

Dicke reports experiences with pancreatic substitution therapy in six children with cystic fibrosis of the pancreas. The diagnosis was established on the basis of infantilism, steatorrhea, and the results of duodenal intubation and of the determination of the amino acid content of the blood. The digestive process of children with pancreatic fibrosis is greatly improved by the administration of pancreas powder during meals. Although it might be assumed that a tablet with an acid-fast cover would be more effective for pancreatic substitution therapy than a pancreatic powder, it was found that in the children with cystic fibrosis of the pancreas a powder was more effective than tablets. Standardization of pancreas powder is essential. The general condition of children with this disorder improves greatly under the influence of treatment with pancreas powder, whereas it has proved impossible to keep them alive with antibiotics alone.

Oversize Fetuses and Their Development After Birth. B. Wennerberg. Nord. med. 56:985-987 (July 12) 1956 (In Swedish) [Stockholm, Sweden].

Of 15,017 children born between 1938 and 1953, 72, or 0.48%, were oversize, with a birth weight of 5,000 gm. (12.1 lb.) or more. The perinatal mortality was almost 10%. If the oversize infants survive the greater risks at parturition, there is no difference between their physical and mental development and that of infants of more normal birth weight, as shown by the follow-up of 59 infants oversize at birth. The parents were of normal weight and height, but in 10 of 51 cases one of the parents had been oversize at birth. There was no case of diabetes among the parents.

Hemorrhagic Diathesis in Children: Follow-Up Examination. T. Friis and P. Pacregaard. Danish M. Bull. 3:108-111 (July) 1956 (In English) [Copenhagen, Denmark].

The prognosis for hemorrhagic diathesis in children is relatively good and seems to be somewhat better in the nonthrombopenic than in the thrombopenic cases. The follow-up examination of 61 children with hemorrhagic diathesis was carried out after an observation period of an average of four and one-tenth years. Only six patients showed signs of tendency to bleeding. Three patients had died, two from hemorrhage.

Hypertrophic Pyloric Stenosis. A. Backman. Nord. med. 56:1026-1028 (July 19) 1956 (In Swedish) [Stockholm, Sweden].

Of 31 cases of pyloric stenosis treated in the children's department of the Maria Sjukhus in Helsinki from 1949 to 1955, 28 were in boys and 6 in girls. The symptoms usually set in during the second or third week of life. In most cases the diagnosis of hypertrophic pyloric stenosis was verified by roentgen examination. Medical treatment was given in 21 cases, with one death, surgical treatment in 13 cases resulted in four deaths. However, the statistics give a wrong picture, as four of the deaths occurred in 1949, when a severe epidemic of diarrhea was raging among infants in Helsinki. When the diagnosis of hypertrophic pyloric stenosis has been established, medical treatment with methyl scopolamine nitrate should be given. At the same time possible disturbances in fluid balance are to be treated. Surgery should not be resorted to unless the medical treatment proves unsuccessful and should preferably be performed in a clinic specializing in pediatric surgery.

UROLOGY

Considerations on the Therapy of Bilateral Lithiasis of the Kidney. M. Sorrentino. Riforma med. 70:729-733 (June 30) 1956 (In Italian) [Naples, Italy].

The author subdivides lithiasis of the kidney into two types, benign and malignant. Benign lithiasis is that type that does not seriously damage the kidney in which the calculi are located and whose effects on the other kidney are not grave. To the group of malignant lithiasis belong those forms that have a rapid and severe effect on the kidney in which they are located and whose effects on the other kidney are severe. Malignancy is determined by the precocity and extent of the lesions, the number of the calculi, the recurrences of the calculosis, and bilateral calculosis. Bilateral lithiasis of the kidney is a systemic disease as well as a disease of the particular organ involved. A general study from the endocrine and metabolic points of view is therefore necessary. Prophylactic therapy is always useful in order to prevent relapses even if it is not possible to detect a definite hyperfunction of the parathyroid. When radiological and laboratory researches indicate a definite hyperfunction of the parathyroid, surgical intervention is advisable. Research to determine whether a lack of vitamin A is present in the blood must always be made. The amount of vitamin A that would be considered sufficient for a normal person would not be so for a person with dysfunction of the liver. Once bilateral calculosis has been demonstrated, surgery should be performed as soon as possible with a method as adequate and as economical as possible. The author has had unexpected results even when he has operated with little or no hope of getting positive results. Nephrectomy should be performed only in cases of extreme necessity. Nephrostomy should be performed, and the calculi should be removed. In case of bilateral lithiasis the more severely damaged kidney should be operated on first. If nephrectomy becomes necessary, the more severely damaged kidney should be removed. The less severely damaged kidney is to be operated on after a length of time depending on the general condition of the patient and the recovery of the kidney that was operated on first. Medical treatment cannnot take the place of surgical treatment, but it can be complementary to it. In the postsurgical treatment the following medicines should be considered: vitamin A, small doses of insulin, drugs for the protection of the liver, liver extracts, kidney nutritive substances, vitamins of the B group, mild diuretics, and large quantities of water.

Anorchism Without Eunuchism. R. D. Amelar. J. Urol. 76:174-178 (Aug.) 1956 [Baltimore].

The case reported concerned a 19-year-old man, who was referred to a U. S. Air Force Hospital for the treatment of supposed bilateral cryptorchism. He was 71.5 in. tall, weighed 141 lb., and had a high-pitched voice. There was no evidence of testes in the scrotal, inguinal, thigh, or perineal regions. Rectal examination revealed the prostate to be small, firm, and symmetrically developed, and the seminal vesicles were not palpable. The impression was that the patient had bilateral abdominal cryptorchism. Bilateral inguinal exploration and an exploratory laparotomy established bilateral anorchism. Acrylic testicular prostheses were inserted into each scrotal cavity for their cosmetic effect. Congenital bilateral absence of the testes is generally considered as synonymous with eunuchism. The psychosexual development of this patient along masculine lines with normal male sexual urges and the ability to have ejaculations is attributed to the occurrence of extratesticular interstitial (Leydig) cells found scattered in islands along the wolffian duct structures in the patient's inguinal canals.

***The Prognostic Significance* of an Elevated Serum Acid Phosphatase Level in Advanced Prostatic Carcinoma.** E. J. Ganem. J. Urol. 76:179-181 (Aug.) 1956 [Baltimore].

A recent clinical investigation of patients with advanced prostatic carcinoma too extensive for cure by radical prostatectomy revealed that 5-year survival rate varied widely from 59% to 0% depending on the presence or absence of hydronephrosis, bone metastases, and an elevated serum acid phosphatase level. These figures applied to patients treated by orchiectomy and estrogenic hormones. The author investigated the influence of acid phosphatase levels on prognosis in 145 patients with advanced prostatic carcinoma. An acid phosphatase level of 3.1 Gutman units or more was considered elevated, and a level of 3.0 or less was considered normal. All of the patients had been subjected to bilateral orchiectomy, and this operation had been followed by treatment with estrogenic hormones. Of 84 patients with a normal acid phosphatase level, 71 did not have and 13 did have metastases; and of the 61 with an elevated acid phosphatase level 33 did not have and 28 did have metastases. The 5-year survival rate among the 33 patients with elevated serum acid phosphatase levels but without demonstrable bone or lymph node metastases was 31% as compared to the group of 71 patients with normal acid phosphatase levels without metastases in whom the 5-year survival rate is 46.8%. The author concludes that if a patient with advanced prostatic carcinoma has no demonstrable bone or lymph node metastases but has an elevated acid phosphatase level, his chance for 5-year survival is significantly less than that of a patient with a normal acid phosphatase level, provided the patient with the normal level is treated by orchiectomy and stilbestrol therapy and survives intercurrent disease. Observations on 28 patients with elevated acid phosphatase levels and metastases further revealed that an elevated acid phosphatase level in patients with bone metastases is a poor prognostic sign and indicates a shorter survival than does a normal acid phosphatase level when the accompanying treatment is bilateral orchiectomy and stilbestrol therapy.

INDUSTRIAL MEDICINE

Treatment of Methemoglobinemia. A. F. Mangelsdorff. A. M. A. Arch. Indust. Health 14:148-153 (Aug.) 1956 [Chicago].

The inhalation of the fumes or dust of the aromatic nitro or amino compounds and the ingestion of or contact by skin absorption with any of these compounds may result in a chemical change of the blood oxyhemoglobin into methemoglobin, the presence of which in the blood stream gives the patient a cyanotic appearance. In mild cases of poisoning caused by aromatic nitro or amino compounds in patients with 30% or less methemoglobinemia a preliminary method of treatment practiced at the medical department of the American Cyanamid Company in Bound Brook, N. J., consists of bed rest, sweetened drinks, advice regarding abstinence from alcoholic drinks, and watchful care. In patients with more than 30% methemoglobinemia a decision is required as to further treatment. Three illustrative cases are described in patients with methemoglobinemia of from 43 to 50%, in whom the methemoglobin blood level dropped below 10% in less than 20 hours and continued to fall, although a "watchful waiting" attitude was assumed and no additional treatment was given. In cases of this type it is, however, necessary to follow the course of the methemoglobinemia by frequently repeated blood samples in order to give additional treatment at once, if necessary.

When the methemoglobin level is above 50%, a method of treatment is used that consists, in addition to the described preliminary treatment, of the intravenous administration of 1,000 cc. of a 5% dextrose solution. Three cases of poisoning caused by *phenylhydroxylamine*, *paranitroaniline*, and *paratoluidine*, respectively, are described in patients with methemoglobinemia of from 50 to 73% whose responses to this method of treatment were characteristic in that the rate of conversion from methemoglobin to oxyhemoglobin was slightly faster when intravenously administered dextrose was used to speed up the normal reversible process. Eighteen hours were required by the "watch and wait" procedure for obtaining a methemoglobin level below 10%. Approximately the same time was required by the method of intravenous administration of dextrose for obtaining the same result, although the original methemoglobin level was higher by approximately 20%.

The case of a seventh patient with poisoning from aniline oil is described. After the preliminary therapeutic procedure had been carried out, his methemoglobin level was still 52%. Ten cubic centimeters of a 1% solution of methylene blue was given intravenously, and five hours were required to obtain a result similar to that obtained with the two other methods of treatment. Because reconversion of mild methemoglobinemia to normal usually occurs within 20 hours, no drastic treatment is necessary. Experimental work carried out by other workers has shown that the indiscriminate use of methylene blue may cause destruction of red blood cells with a resulting progressing anemia and that some of the blood pigment may become lodged in the kidney or urinary bladder. Methylene blue or other reducing compounds should, therefore, be used only in severe cases of methemoglobinemia and then with caution.

The Promazine Treatment of Alcoholism: A Preliminary Report. F. A. Figurelli. Indust. Med. 25:376-380 (Aug.) 1956 [Chicago].

Chlorpromazine is likely to induce severe hypotension, and this is especially serious in view of the unstable vasomotor mechanism of the alcohol addict. There is a definite risk of a precipitous fall in blood pressure in the acutely inebriated if more than 50 mg. of chlorpromazine is administered over a four-hour period. Parkinsonism has been observed after the continuous administration of chlorpromazine; patients complain of severe pain after intramuscular injection; and allergic cutaneous eruptions have been the source of complaints. These and other factors induced the author to try promazine (dimethylamino-n-propylphenothiazine), which is said to produce similar pharmacological effects but less intoxication than chlorpromazine. It is now realized that the chlorine radical is unnecessary for the ataractic effect.

The author presents observations on 54 consecutive unselected clinic patients (48 men and 6 women) in whom promazine was used in the treatment of alcoholism. All had been drinking a number of years. Many had been admitted on several previous occasions, sometimes as often as three or four times a year. Twenty-four had active and 16 impending delirium tremens. The other 16 were acutely inebriated. Some were noisy, belligerent, and difficult to manage; others were tremulous, nervous, and nauseated, or drowsy and stuporous, later becoming violently active. The first 13 patients received the routine treatment for alcoholism initially (laxatives, high colonic irrigations, conventional sedatives), and two were given chlorpromazine by mouth, with no results. Promazine therapy was then instituted. In 39 promazine therapy was started immediately on admission; no other medicaments were used. The dose of promazine was standardized at 100 mg. by mouth four times a day. Five of the acutely inebriated patients recovered after only two doses of 100 mg. administered over a 12-hour period (overnight). They slept soundly and were able to return to their jobs the following morning. Nine patients required three to seven doses. These, too, slept throughout the night and were discharged late the following day in condition to resume work. Thirty-one patients required from 8 to 16 doses over a period of from two to four days. Ten patients who were violently ill and suffering from severe complications required 19 doses or more. Two of these (one with Korsakoff's syndrome and one with cirrhosis of the liver), both of whom had pneumonia and asthma, remained under treatment for 10 and 12 days, respectively, after which they were transferred to other wards for further treatment of their medical problems. The average duration of acute symptoms was 2.1 days and the average hospital stay 3.3 days. There were no side-effects. All were able to return to work unless prevented by complicating illnesses. Promazine is non-habit-forming and may be used by the family physician for the care of the alcoholic at home. Alcoholism can now be treated in the general hospital and delirium tremens in the regular medical wards.

THERAPEUTICS

Palliation of Carcinomatosis with Ascites by Means of Hemisulfur Mustard (2-Chloro-2'-Hydroxydiethyl Sulfide). A. M. Rutenburg and A. M. Seligman. New England J. Med. 255:361-368 (Aug. 23) 1956 [Boston].

A preparation of 2-chloro-2'-hydroxydiethyl sulfide (hemisulfur mustard) was administered to 30 patients with inoperable cancer. Patients selected for treatment were inoperable and unsuitable for radiation or had received the maximum dose of radiation or had become refractory to further radiation therapy. Most of the patients were in the terminal stage of their disease. All had either palpable masses readily accessible to biopsy or other objective evidence of the extent of their disease such as ascites, pulmonary or skeletal metastases, or tumor cells in the peritoneal or pleural exudate. Hemisulfur mustard was supplied in solution in dry ether in sealed glass ampuls, which were stored at —10 to —20 C. The concentration in each batch of ampuls varied from 90 to 120 mg. per milliliter. At the bedside the dry-ether solution equivalent to about 100 to 400 mg. of hemisulfur mustard was withdrawn with a needle and syringe from the ampul and immediately added to 50 ml. of sodium chloride solution (0.85%) and vigorously agitated by aspiration with some air into a 50-ml. syringe. The resulting opalescent solution was then rapidly injected (within 60 seconds) through polyethylene tubing that had been inserted into the superior vena cava via the brachial vein. After the injection the tubing was flushed with sodium chloride solution (0.85%). The polyethylene tubing was kept patent by the injection of heparin.

The toxic reactions seen after treatment consisted of nausea, vomiting, malaise, and tremor. Fourteen of the 30 patients treated were temporarily benefited. The best results were achieved in patients with ovarian carcinoma and peritoneal carcinomatosis and in one patient with a mixed mesodermal tumor of the endometrium. Palliation consisted of decreased formation of ascites, decrease in size of tumor masses, decrease in pain, and increase in appetite, strength, and sense of well-being. The longest remission of symptoms observed in one patient was 29 months.

Psychoses After Barbiturate Acid Antidote (Megimide, Glutamisol). J. Kjaer-Larsen. Ugesk. laeger 118:768-773 (July 5) 1956 (In Danish) [Copenhagen, Denmark].

Psychoses after administration of Glutamisol, which have not been described previously, occurred in 15 of 50 patients treated with this agent for acute barbiturate intoxications. The psychoses resemble spontaneous abstinence psychoses and were seen mainly among misusers of barbituric acid and in some patients with long-continued acute intoxication following administration of therapeutic doses of barbituric acid, most often after large doses of Glutamisol. The psychoses are regarded as exogenic reactions provoked by Glutamisol. While benign, they were unpleasant experiences for both the patients and their families. The risk of psychosis does not constitute a decisive contraindication for Glutamisol, but calls for observance of strict indications and particularly for care in the case of misusers of barbituric acid.

Experiences with Megimide in Treatment of Barbituric Acid Intoxication. A. Louw and L. M. Sonne. Ugesk. laeger 118:761-768 (July 5) 1956 (In Danish) [Copenhagen, Denmark].

In Bispebjerg Hospital, from September to December, 1955, 24 patients, aged from 24 to 82, with grave barbituric acid intoxication were treated with Megimide given by intravenous infusion. Most of the cases were pure barbiturate intoxications. Almost all the cases were grave, as evidenced by the clinical condition and the barbituric acid content in the blood. Megimide proved to be a potent stimulant of reflex activity and respiration and an important agent for bringing the patients into a safe state. It did not shorten the duration of coma or increase the rate of elimination of barbiturate from the blood. In three cases there were light, transient attacks of tonic-clonic convulsions and in six cases transient psychic disturbances appeared from one to three days after return of consciousness. Megimide may possibly have both an antidotal effect and an effect through cerebral stimulation. It does not cause the increased blood pressure or hyperpyrexia seen on application of central analeptics and does not seem to lead to increased oxygen consumption in the brain tissue. It can therefore be regarded as a valuable addition to the agents available for the treatment of hypnotic intoxication.

RADIOLOGY

Infantile Arteriosclerosis. H. S. Weens and C. A. Marin. Radiology 67:168-174 (Aug.) 1956 [Syracuse, N. Y.].

Approximately 40 cases of infantile arteriosclerosis have been reported, but the large majority of these cases were discovered at autopsy. The authors report clinical, radiological, and pathological studies on two infants with arteriosclerosis. A boy was hospitalized at the age of 10 months because of progressive loss of weight and enlargement of the abdomen. The essential findings on physical examination were emaciation, abdominal distention, and a small umbilical hernia. Roentgenograms of the long bones revealed a delicate but widespread calcification of the arteries that was most pronounced throughout the soft tissues of the forearm and lower extremities. Hypertension was demonstrated. After discharge and improvement, the child was readmitted at the age of 16 months with edema of the lower extremities. Emaciation and abdominal distention had progressed considerably. In spite of supportive therapy, the patient died on the fifth hospital day. At autopsy the heart showed marked hypertrophy of the left ventricle. On microscopic examination, the medium-sized arteries of the heart showed a patchy calcification of the media, with intimal proliferation leading to diminution of the vascular lumina. Various degrees of fragmentation were noted in the internal elastic membrane of these vessels. The predominant cause of death in the second infant appeared to have been an intracranial hemorrhage. It remains conjectural to what extent the widespread arterial disease contributed to the intracranial complications and fatal outcome. The case showed that the arterial changes may be demonstrated on the roentgenograms of the upper extremities.

Infantile arteriosclerosis has been recognized in renal disease, hyperparathyroidism, and vitamin D intoxication. Similar arterial changes have also been noted in progeria, in which the arteriosclerotic process is associated with extensive growth disturbances and profound metabolic changes. Infantile arteriosclerosis has been observed also in children in whom no obvious etiological factors were apparent. The principal morphological changes of the arteries in these children are a disorganization of the internal elastic membrane accompanied by deposition of lime salts in its proximity. Concurrently a marked fibroblastic proliferation of the intima takes place, which may attain such proportions that the involved vascular lumen becomes markedly narrowed or even obliterated. The majority of children with this disorder were less than a year old or even newly born. The onset of symptoms was often sudden, particularly in those with severe coronary artery disease; they had cyanosis, dyspnea, and lethargy suggesting acute cardiac failure. In others, in whom there was a more subacute or chronic course, the clinical picture was largely that of impaired health with anorexia, vomiting, weight loss, and general debility. The clinical symptoms are not usually characteristic enough to permit a diagnosis of this disease entity, but the roentgen examination should make it possible to recognize the condition during life. In all cases of unexplained heart failure and cardiac enlargement in infancy and childhood, as well as in debilitating diseases of unknown etiology, calcification of the arteries should be searched for by proper radiological studies.

The Roentgen Aspects of Necrotizing Renal Papillitis. R. E. Ottoman, J. H. Woodruff Jr., S. Wilk and F. Isaac. Radiology 67:157-167 (Aug.) 1956 [Syracuse, N. Y.].

Acute necrosis of the renal papillae has been described under a number of different terms such as "renal papillary necrosis," "renal medullary necrosis," "necrotizing papillitis renis," and "Günther's necrosis." It occurs most frequently as a complication in patients with diabetes mellitus and acute pyelonephritis. Less frequently it complicates obstructive uropathy with superimposed infection. Ottoman and his associates review the roentgenologic observations reported in the literature and report their own studies on eight patients in whom they performed pyelography. The onset of complicating papillary necrosis should be suspected in any patient with diabetes mellitus or obstructive uropathy whose clinical condition suddenly becomes worse and in whom there is a decrease in urinary function and a rapid rise in the blood urea nitrogen level. Laboratory studies usually reveal microscopic or gross hematuria, albuminuria, glycosuria in the diabetics, bacilluria, frequently decreasing urinary function, and a rising blood urea nitrogen or nonprotein nitrogen level.

A film of the abdomen with the patient supine will show enlarged outlines, which, however, will also be seen in a number of other disorders. The value of the excretory urogram is limited, because of the poor renal function associated with papillary necrosis, but the process has been demonstrated with the aid of adequate lower abdominal compression. Retrograde pyelography is the method of choice. This procedure can best be relied upon to fill any fistulas or channels and to demonstrate the degree of cavitation or sequestration. As bland an opaque medium as possible should be used, with only low-grade pressure, in filling the urinary tract, so as not to precipitate necrosis within inflamed papillae. The eight patients with necrotising renal papillitis subjected to pyelographic studies showed the following roentgenologic changes: calyceal haziness or lack of sharpness; ulcerative or erosive papillary changes; intramedullary or intrapapillary, (ring shadow) sinus formation; parenchymal cavitation with communicating sinuses; amputated calyces; extruded papillae with secondary club-like papillary fossa, ureteral or calyceal obstruction, or intrapelvic filling defect; narrow infundibula, occasionally showing a "moth-eaten" margin; decreased urinary function (in the intravenous pyelogram); and enlargement of the renal silhouette. Diagnosis of necrotizing renal papillitis can be made with a considerable degree of accuracy by retrograde pyelography and more exactly by histological examination of portions of the sloughed papilla either passed in the urine or found in the bladder in the course of cystoscopy. Earlier and more frequent recognition of this complicating process will permit more prompt institution of effective therapeutic procedures.

BOOK REVIEWS

Anatomy for Surgeons. Volume 2: The Thorax, Abdomen, and Pelvis. By W. Henry Hollinshead, Ph.D., Professor of Anatomy, Mayo Foundation, University of Minnesota, Rochester. Cloth. $20. Pp. 934, with 1109 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1956.

This book is an anatomic presentation of regional anatomy of the thorax, abdomen, and pelvis, designed for the student of surgery—pupil or master. The author attempts to present a mixture of classical anatomy flavored with a discussion of "those details upon which the more mature surgeon, consciously or unconsciously, bases his daily work; second, to provide for the more mature surgeon a refresher for those details which are, perhaps, slightly outside his own field of interest, and a source of ready reference to the details which, although lying in his own field, he cannot expect to keep constantly in mind." Each chapter has been organized so that it can be read as a whole or in part, depending on the surgeon's immediate requirements. Volume 1, on the head and neck, accomplished this purpose admirably; it was reviewed in The Journal (157:400 [Jan. 22] 1955).

Although the author achieves fairly well what he sets out to do, there are certain areas in which more extensive illustrations would be useful, even to the mature surgeon, especially on the subjects of the breast and the alimentary tract with reference to the lymphatic distributions in particular. He has not taken advantage of the more recent observations on the breast by Handley (1954) and the observations on the lymphatic and venous drainage of this organ as related to the radical or extended radical mastectomy. The illustrations of the trachea and bronchial tree, the pulmonary segments, the heart, and the great vessels are presented in greater detail and with more recent references than are those of the breast. The vagus nerves are discussed and illustrated, but with a few surgical features not clearly presented or well illustrated. The abdominal wall and inguinal region are well described and accurately illustrated, especially inguinal hernia, although more detailed and less schematic drawings would be useful in a few instances. The abdominal viscera and peritoneum are accurately described but lack practical illustrations bearing on surgical incisions, operative exposures to the subphrenic spaces, and the lesser peritoneal cavity, spleen, pancreas, stomach, and colon. This may be more disadvantageous to the student than to the mature surgeon. On the other hand, discussion and illustrations relative to the treatment of portal hypertension and the biliary tract are more extensive and very helpful. The blood supply to the stomach, duodenum, spleen, liver, small intestine, and colon is well illustrated. Gerota's fascia and its relationship to the kidney is discussed but unfortunately not well enough illustrated to be easily understood. Renal anomalies are extensively discussed and illustrated, as is the rest of the genitourinary tract, except for the surgical landmarks essential to identification of the ureters from various surgical exposures. The rectum is described and illustrated according to past prevailing views; the very recent British work is not included, however. The chapters dealing with the perineum, prostate, and female pelvis are adequate.

The text suffers less than the illustrations. The latter in many instances are too schematic to be as useful as required by most surgeons. Preceding the text of each chapter is a full-page illustration of the region under discussion. None of these are labeled, which limits their value largely to one of decoration. The text, too, suffers slightly by comparison with that of volume 1, for, in the extensive use of references in this volume, the author loses to some extent the basic and established principles of anatomy in the more elaborate discussion of some of the less important and controversial areas. However, the references to such works serve as useful guides to the surgeon wishing more detailed information. With the growing interest in the surgery of cancer, the surgeon often searches for a discussion and illustration of the lymph glands and the lymphatic circulation as a whole. Although the lymphatics are discussed regionally, it would be helpful if the subject were dealt with in its entirety. This book can be recommended as a reference for the surgeon, but until revised it does not equal some other similar textbooks.

A Manual of Practical Obstetrics. By the late O'Donel Browne, M.B., M.A.O., M.A. Edited and largely rewritten by J. G. Gallagher, M.D., M.A.O., F.R.C.P.I., Assistant Gynaecologist, Mater Hospital, Dublin, Ireland. Third edition. Cloth. $7.50. Pp. 265, with 203 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2; John Wright & Sons, Ltd., 42-44, Triangle West, Bristol 8, England, 1956.

This is a compendium-type book designed for the general practitioner in Ireland. The original edition was published 20 years ago by Browne; the present edition has been revised by Gallagher. During and following World War II, there appeared in the American market numerous specialty compends, which were useful mainly as outline reviews for young men deprived of the detailed larger textbooks and for a quick "brush-up" for specialty and state-board examinations. For the American physician, these are preferable to the volume reviewed. Drugs not in common use in America are recommended by name, whereas general terms, such as a mild sedative, an antiseptic solution, a sulfonamide, or an antibiotic, would have been preferred. The single doses of pituitary extract suggested for inducing labor are far too large, and the use of seaweed tents and bougies to induce labor should be abandoned. Line drawings in reasonable number illustrate the text, but no readily discernible reason exists for showing one forceps blade applied with the patient in the lateral prone position, the other with her in the dorsal position. The book is not recommended for use in America.

Borderlands of the Normal and Early Pathologic in Skeletal Roentgenology. By Prof. Dr. Alban Köhler. English translation arranged and edited by James T. Case, M.D., D.M.R.E., Director, Memorial Cancer Foundation, Santa Barbara, Calif. Tenth edition by Dozent Dr. E. A. Zimmer. Cloth. $24.50. Pp. 723, with 1282 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 99 Great Russell St., London, W.C.1, England, 1956.

This book is a real classic in the field of skeletal roentgenology. Dr. Zimmer, always preserving the Köhler tradition, has ably rewritten and augmented the 10th edition. The fact that this is the 10th edition and that there are translations into French, Spanish, and Italian indicates the wide significance of this work. It is difficult to conceive of any normal or variant of normal pertinent to the skeletal system that is not included here. All the conditions are well illustrated, with concise captions. The bibliography has been augmented by Dr. Case to include appropriate references to English-language periodicals. This book is a joy not only to the radiologist but also to any physician, particularly the orthopedist, interested in trauma and diseases of the skeletal system. The basic and fundamental importance of the information so completely compiled in this work cannot be overemphasized and makes the book an essential reference work for any medical library.

Physical Diagnosis. By Ralph H. Major, M.D., Professor of Medicine and of History of Medicine, University of Kansas, Kansas City, and Mahlon H. Delp, M.D., Professor of Medicine, University of Kansas. Fifth edition. Cloth. $7. Pp. 358, with 536 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, England, 1956.

This edition appears five years after the fourth edition. The chapter on history-taking has been placed, appropriately, at the beginning of the book. In a subject as vast as that of the approach to the patient, there are bound to be minor omissions, but, in general, this textbook covers the field adequately. The paper is good, the illustrations are well reproduced, and typographical errors are few. This textbook may be recommended.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

QUERIES AND MINOR NOTES

NOISE IN INDUSTRIAL PLANT

To the Editor:—*An industrial plant using hammers and forging equipment is considering an investigation of the hearing of employees. Their surgeon has asked for help in outlining a program for the examination of employees and also alleviation of some of the noise.*

M.D., Pennsylvania.

Answer.—Medical supervision of workers exposed to excessive noise involves careful examination, employee counseling, and proper job placement. Examination should be made prior to employment, periodically thereafter, and at time of termination to determine and record existing hearing loss and related disorders. Permanent records should be made. Prior to the original examination it is desirable to obtain a detailed history from the applicant, inquiring particularly into noise exposures in previous jobs as well as in military service. The medical phase of the inquiry should embrace aural pain, drainage, ear injury, surgery (ear or mastoid), head injury with unconsciousness, tinnitis, and deafness in the immediate family.

Medical examination requires more than usual attention to malformation of the external ear or canal, obstruction or drainage, perforation or scarring of drumhead and obstruction of the eustachian tube, supplemented by subjective tests of hearing acuity. Pure tone audiometry by air conduction only is used in making industrial screening tests. Screening examinations for placement purposes involve tests of hearing thresholds at the following frequencies—500, 1,000, 2,000, 4,000, and 6,000 cps. Most audiometers include frequencies of 125, 250 and 8,000 cps, but these are not essential for industrial needs. A permanent record (audiogram) should be made of each audiometric test, properly identified as to name of subject, date, and name of person giving test.

In audiometric testing, best results indicative of true hearing acuity are obtained if tests are made before the beginning of noise exposure. This would be at the start of the shift and, even better, after a week end away from work. This is due to temporary threshold shift, in which the hearing acuity is poorer after exposure to noise and better after some hours of absence from noise. Therefore, the true base line of acuity (and loss, if any) should be established under the most accurate conditions, whenever possible. The room in which audiometric testing is conducted must be as free from noise as possible, in order that some sort of standard testing conditions are established. There is little or no masking effect if ambient noise in the test room is kept below 50 db. A test room with 40 db. of ambient noise is preferable. In many industrial situations it will be difficult to find such a suitable room, and it may be necessary to construct a special room for this purpose. Prefabricated quiet rooms are available commercially.

Transfer of a worker from a non-noisy job to one that is potentially harmful should be preceded by an examination conducted with the same detail as a preemployment examination. Periodic examinations of workers are important after placement in a noisy environment. These periodic tests may be confined largely to audiometric tests for detection of early evidence of hearing damage or fatigue due to previously unsuspected sensitivity. Reexaminations should be made about 30 days after placement, to test for possible early effects of noise, and at semiannual or yearly intervals thereafter. The physician should interpret and evaluate the various medical data relating to each individual. He should determine the existence of hearing loss or pathological disorders of the ear, the need for referral to the worker's personal physician or to an otologist, the desirability of rehabilitation through the use of hearing aids, vocational or other training, and proper job placement of workers. The applicant with a detected hypersensitivity to noise should not be so exposed, whereas the otherwise qualified deaf individual would be ideal because of the absence of any possibility of further damage to his hearing.

The ideal method of preventing noise damage to the ear is by control or reduction of the noise at its source by engineering methods. This is often difficult to achieve in industry and requires the best engineering talent as well as considerable ingenuity. Noise measurement and analysis are essential steps in the control endeavor. When noise control is not feasible or is only partially successful, it may be necessary to resort to protection of the workers through the use of suitable ear plugs, ear muffs, or helmets. Personal protective devices designed to reduce the amount of noise reaching the auditory nerve also call for medical supervision. This is especially true of those devices that must be placed in the auditory canal. Sanitation and personal hygiene require that such devices be personal. In addition to advising on the hygienic problems involved, the physician may also aid in the education program that will be necessary to get full acceptance from the workers of the need for noise protection.

CONTROL OF ALGAE IN SWIMMING POOLS

To the Editor:—*What is the best algicide for use in a swimming pool? It does not have to be anything that is used repeatedly, because we usually change the water every week.*

Darius Gray Ornston, M.D., Philadelphia.

Answer.—Many chemicals are marketed for control of algae in swimming pools. Their effectiveness as algicides depends frequently on the amount used, the method of application, and the particular kinds of algae present. One of the algicides commonly used is copper sulfate, but it must be applied correctly and in the right concentration. If the algae are distributed through the water and not attached to the sides or bottom of the pool, the copper sulfate can be placed in a loose bag such as one made of burlap. The bag is then dragged or moved through the water just below the surface until the algicide has dissolved. About 2 ppm of commercial copper sulfate is sufficient to control the common planktonic algae found in many swimming pools. By applying 2.5 oz. by weight of copper sulfate for every 10,000 gal. of water in the pool, approximately that concentration is obtained. The treatment is most effective if applied before the algae become so abundant as to be visible. Where the water in the pool is changed each week, one treatment each time the pool is filled would be adequate. For control of algae attached to the walls, a treatment is applied when the pool is drained. As much of the growth as possible is scrubbed off, and then the walls are sprayed with a 5% solution of commercial copper sulfate.

The active ingredients in other algicides include such chemicals as chlorine, 2,3 dichloronaphthoquinone, quaternary ammonium compounds, rosin amines, colloidal silver, and 3-(p-chlorophenol)-1, 1-dimethylurea. Information available from local health authorities should be useful in determining the kind of algicide and the treatment permitted or recommended for swimming pools in any one locality.

MATERNAL OXYGEN AND FETAL DISTRESS

To the Editor:—*It is a common obstetric practice to administer oxygen to the mother if fetal distress develops during labor, the rationale for this being that presumably increased concentration of oxygen helpful to the fetus results. Are there any factual or experimental data to support this?*

Joseph Rini, M.D., Springfield, Mass.

Answer.—The oxygen administered to the mother is taken up by the blood plasma. The amount of increase is about 2%, but this is apparently sufficient to favorably affect the baby in utero.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

SODIUM-FREE DIET

To the Editor —*How long a period of time may a person be kept on a complete sodium-free diet? A patient with congestive heart failure has been on a sodium-free diabetic diet for many months without any significant side effects He is taking also digoxin, 0 25 mg three times a day, aminophylline, 0 2 gm three times a day, quinidine, 0.2 gm three times a day, and potassium chloride, 10 grains twice a day If sodium chloride is so important for the physiological process, why does this man have no complications from the above-named diet?*

Julian Mowchan, M D , Oakwood, Ohio

Answer —Among animals only a few ungulate species seek salt outside the diet Some persons theorize that man should live like the great majority of animals and that the use of added salt is abnormal and even harmful When necessary, the resorptive power of the kidneys can conserve sodium so that practically none is lost in the urine, and the elimination by skin and intestine is covered by the salts of natural foods When there are excessive losses, as with profuse perspiration from heavy labor in a hot environment or, less often, with severe diarrhea, extra salt ingestion is necessary to save life Otherwise, the great mass of patients live comfortably on the most rigid sodium restriction even in hot weather The drugs mentioned will not interfere, but drastic diuretics such as the mercurials might create serious salt deficiency

ITCHING AFTER A SHOWER

To the Editor —*Immediately after taking a shower, a patient develops violent itching all over the body with no rash, lasting about 30 minutes Physical examination is negative, except for a history of allergy What treatment would be of value in this condition?*

Harry R Deane, M D , St Petersburg, Fla

Answer —A generalized itch occurring immediately after bathing may be due to a number of causes, among which may be mentioned hypersensitivity to heat, cold, type of soap used, hardness of water, dryness of skin, and time of year, especially during cold weather

Treatment should be along the following lines 1 Take an antihistamine in appropriate dosage one-half hour before bath 2 Rub mineral or vegetable oil over affected areas before bathing 3 Change temperature of water used If cold baths have been taken, change to warm If relieved, gradually take cooler baths and vice versa 4 Eliminate soap or change soap used or limit soap to areas such as groin, axillas, and feet 5 Take tub baths for a time, using water containing a soothing agent such as starch or oatmeal 6 If skin feels dry, apply twice daily an ointment containing some lanolin or similar product Hydrocortisone ointment or some similar steroid product may be used sparingly and only in severe cases

RETINITIS PIGMENTOSA

To the Editor —*Please discuss retinitis pigmentosa When senile cataracts accompany the condition should they be removed? What improvement in vision might be expected by their removal when retinitis pigmentosa has been present for many years?*

M D , New York

Answer —Retinitis pigmentosa is an abiotrophic degeneration of the outer layer of the retina (rod and cone units) that usually begins in childhood and usually, but not always, progresses unremittingly to blindness Central vision is usually retained until the last The disease has wide variation in its course and manifestations, several subtypes are included under the name of retinitis pigmentosa It is usually transmitted as a Mendelian recessive trait, but vitamin A deficiency and several toxic agents induce an end-stage similar to that of retinitis pigmentosa (iodoacetate) There is no time-tested effective treatment for it although various medicaments have been recommended from time to time, Dicumarol is the most recent of these (Leo and Lidman. *Am J Ophth* 39 46, 1955) Whether a patient will profit by removal of senile cataracts depends on the extent of retinal disease and on the maturity of the cataracts This would necessitate ophthalmologic evaluation of each case individually.

FRACTURE OF NAVICULAR AND RADIUS

To the Editor —*A 62-year-old woman was seen recently who had fallen and injured her left wrist X-ray examination revealed recent fractures of both the navicular bone and the distal end of the radius on the same wrist I have never seen these fractures occur together and can find no mention of it in the standard textbooks on fractures I am treating the wrist as though the navicular alone had been broken, since my feeling is that this bone is likely to cause more trouble*

Donald Meehan M D , Springville, N Y

Answer —If there is no displacement of the lower end of the radius, healing should take place without complications but it will require considerably more time than for a simple fracture of the radius Immobilization in dorsal flexion and radial adduction at the wrist with a light, smoothly applied, volar, molded plaster splint would be the treatment of choice The abducted thumb should be included in the splint, but the splint should stop short to permit movement at the metacarpophalangeal joints of the fingers and at the interphalangeal joint of the thumb

STABILITY OF PENICILLIN

To the Editor —*To what degree is the potency of procaine penicillin reduced by carrying vials in the physician's bag during summer? How long, in the matter of days, after having been in such a bag should a multiple dose vial of penicillin be discarded?*

M D , Ohio

Answer —Procaine penicillin in aqueous suspension is relatively stable Tests show that it does not lose significant potency after being held at 98 F (37 C) for periods of up to three months Even at temperatures of 48 C this preparation does not lose significant potency for a period of three weeks For all practical purposes, this drug may be carried during the entire summer in a physician's bag without fear of loss of significant potency However, even though little or no loss of potency occurs, this preparation may thicken after prolonged holding at high temperatures, markedly decreasing syringeability Procaine penicillin in oil with aluminum monostearate and dry procaine penicillin powder for injection are even more stable than procaine penicillin in aqueous suspension

SERUM IODINE LEVEL DURING PREGNANCY

To the Editor —*It has been said that elevated protein-bound iodine levels are to be expected in pregnancy Are data available concerning the time that this increase occurs, its variance during the pregnancy, and the rate of return to normal post partum?*

Wallace C Ellerbroek, M D , Long Beach, Calif

Answer —The normal values of serum precipitable iodine during pregnancy range between 6 2 and 11 2 mcg per 100 cc The normal range in nonpregnant women is 4 to 8 mcg per 100 cc This elevation is physiological and is noted as early as three weeks after conception It does not increase as pregnancy advances It drops to the normal range after delivery (Man and others *J Clin Invest* 30 137, 1951)

BAROMETRIC PRESSURE AND THE ONSET OF LABOR

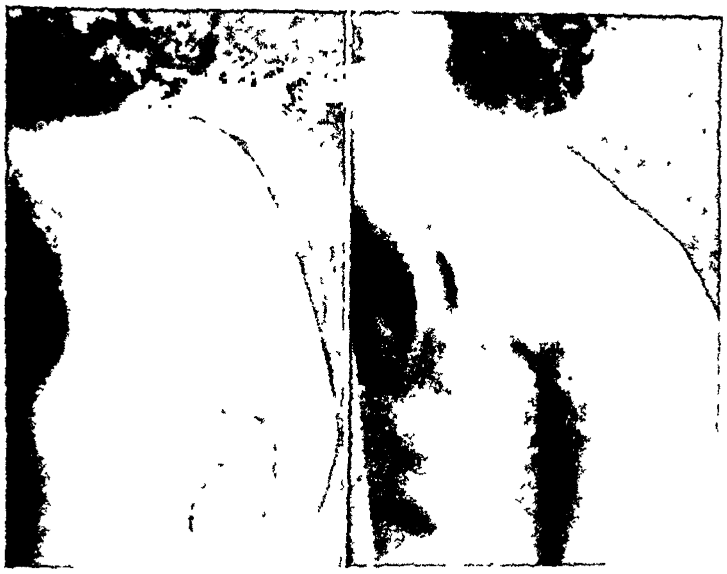
To the Editor —*Observation of many obstetric patients in two large hospitals has indicated that there appears to be some correlation between the onset of labor in patients at term and near term and a sudden marked fall in atmospheric barometric pressure Also it is known that in Leadville, Colo (2 miles above sea level), there is a high rate of premature births (highest in the United States) Surely the low barometric pressure is playing a role here Have others observed this phenomenon?*

V L Hicks M D , Kansas City, Mo

Answer —There is no proved association between a fall in barometric pressure and onset of labor. A sudden change of weather may, however, lead to a sudden apparent onset of or an increase in severity of preeclampsia and eclampsia.

TROPHIC ULCERS FOLLOWING HEAVY IRRADIATION

To the Editor:—*In reference to a query that appeared in the June 23, 1956, issue of* The Journal, *page 774, under the title of "Trophic Ulcers Following Heavy Irradiation," I wish to advise that it is not always true that skin grafting over these areas will consistently fail. We have had a number of successful cases. A woman was first operated on in 1941, elsewhere, for adenocarcinoma, grade 3, of the left breast, with metastasis to the axillary lymph nodes. This lesion had existed for one year prior to surgery. In March, 1942, she had extensive local recurrence in the axillary region in the upper end of the surgical scar, with supraclavicular nodes that extended to the sternomastoid junction making surgery impossible, even an intrascapular thoracic operation. With the patient's consent, she was given excessive deep x-ray therapy. In 1950 the irradiated areas began to break down and ulcerate, with extensive hyperkeratosis. Wide excision of involved skin was carried out at three subsequent operations with immediate skin graft. The figure shows recent pictures of the results. I am afraid that, if the query referred to above is taken literally, some patients will be denied relief of this distressing condition. I do not mean that it should be carried out in all cases, but there are certain instances where resection and skin graft can be used.*



Skin grafts of patient after excision of ulcerated skin areas due to irradiation.

Dudley Jackson Sr., M.D.
1525 Nix Professional Bldg.
San Antonio, Texas.

TREATMENT OF CARDIOSPASM

To the Editor:—*I would like to comment on the answer to the question on treatment of cardiospasm, in the July 7, 1956, issue of* The Journal, *page 1034. The fact that the patient had cardiospasm for 20 years does not necessarily indicate that the esophagus is greatly dilated or angulated. If the organ is not angulated, unguided tubes such as Hurst dilators may be passed through the cardia into the stomach, but this seldom provides significant relief from symptoms. When the esophagus is dilated and angulated, Hurst dilators, or any other unguided instrument, will not enter the cardia but will press against the redundant wall of the most dependent portion of the esophagus, frequently at a lower level than the entrance into the stomach. Undue pressure may result in perforation of the esophageal wall.*

Esophagoscopy in a patient who suffers from cardiospasm may be a distressing procedure as a result of retained secretion in the esophagus, and if the organ is widely dilated and angulated the opening into the stomach may be difficult to identify. Even when the esophagoscope can be passed into the stomach, the degree of dilation of the cardia is seldom sufficient to provide even temporary relief from dysphagia. One dilation of the cardia with a hydrostatic dilator guided into the stomach by a previously swallowed silk thread will give complete and permanent relief from dysphagia in 75% of patients who suffer from cardiospasm. The other 25% may have occasional catching of food at the cardia and some may require subsequent dilation, but all can be given sufficient comfort so that other operative procedures are not required. Failure to relieve cardiospasm when using the Russell hydrostatic dilator indicates that the instrument was not maintained in proper position when being distended with water.

Porter P. Vinson, M.D.
Medical College of Virginia Hospital
Richmond, Va.

To the Editor:—*The reply to the question on the treatment of cardiospasm in Queries and Minor Notes in* The Journal, *July 7, 1956, page 1034, seems inadequate, in that too much emphasis is placed on mercury-weighted tubes, which are of little value, and insufficient attention is paid to more effective nonsurgical methods of dilating the cardia. Olsen and co-workers* (J. Thoracic Surg. *22:164, 1951), using metal bougies and hydrostatic bags employing pressures to 9.5-10.3 lb. per square inch, reported a satisfactory result in 60.2% of 601 patients treated with one course of dilation and 69.2% after one or more courses. Ten per cent of the patients were relieved of symptoms permanently with the use of metal bougies only. Vinson (Diagnosis and Treatment of Diseases of the Esophagus, Springfield, Ill., Charles C Thomas, Publisher, 1940) obtained similar results; subsequent dilation provided permanent relief for almost all. Esophagoscopy is rarely needed to carry out the dilation. Fluoroscopic aid may be of definite value in the location of the bag. Crump and co-workers* (Gastroenterology *20:30, 1952) use a metal dilator guided into the stomach by piano wire. It is then withdrawn to the cardia and the blades forcefully opened. The results in 72 patients were satisfactory after the first dilation in 82%. Ninety-five per cent were permanently relieved of symptoms after one to three dilations.*

The complications of the procedure, i. e., esophageal "splitting," aspiration pneumonitis, and hematemesis, are about 3%; the mortality is negligible. Except in children less than 10 years old results are comparable in all age groups. There is no relation between duration of symptoms and expected result. There is little or no relationship to the degree of esophageal deformity as seen fluoroscopically except in extreme dilation and tortuosity. No regression in the deformity can be demonstrated fluoroscopically after complete relief of symptoms; the motor function of the lower two-thirds of the esophagus remains impaired.

The experience of one of us (W. L. P.) is with the pneumatic dilator, still preferred, even though the statistical reports seem to favor the hydrostatic and metal dilators. The chief point of this comment is that the preferred and, indeed, if properly performed, almost routinely satisfactory method of treatment for cardiospasm is dilation of the cardia by the nonsurgical measures mentioned. It may be appropriate to mention that the Heller operation, although a splendid procedure when indicated, carries some element of risk. Experience has shown, furthermore, that postoperative regurgitation into the esophagus with peptic ulceration, stricture formation, and shortening of the esophagus, can develop.

Walter L. Palmer, M.D.
Philip A. Christiansen, M.D.
The University of Chicago
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Chicago 37.

« Washington News »

Medical Care for Military Dependents • •
Jenkins-Keogh Proposal Revived for Next Congress • •
Burney Announces PHS Top Personnel Shifts • •
Foreign Service Openings for Public Health Nurses • •
Venereal Disease Program Moved to Atlanta, Ga. • •

MEDICAL CARE FOR MILITARY DEPENDENTS

By now 24 state medical societies have completed, or are in the process of, negotiation of contracts with the Defense Department for providing medical care to dependents of uniformed personnel. Society representatives bring to Washington a model local fee schedule, with at least 200 of the 700 items filled in with charges suitable to their areas. This is checked over with Defense Department officials, as are other provisions of the model contract. State societies are not required to accept all provisions of the contract drawn up by the Defense Department but are free to negotiate for any changes that would be more suitable in their particular situation.

When the program goes into effect Dec. 7, fiscal or disbursing agents selected by the state societies will be in charge of handling billings from physicians and making payments to them from Defense Department funds. To date the following state societies have completed or have started their contract negotiations: Michigan, California, Washington, Colorado, New York, Minnesota, Indiana, North Carolina, Oregon, Connecticut, Wisconsin, Massachusetts, Maryland, New Jersey, New Hampshire, Vermont, Rhode Island, Iowa, Illinois, Nebraska, and Montana.

REVIVAL OF JENKINS-KEOGH PROPOSAL

One of the sponsors of the long-standing Jenkins-Keogh proposal for establishment of individual tax-free pension plans has been laying groundwork for a revival of the legislation in the next Congress. Rep. Eugene Keogh (D., N. Y.) has written his colleagues in Congress urging them to endorse the proposal during their election campaigns. When the next Congress convenes the bill will be reintroduced, possibly with an amendment to permit a "take-down" of funds, Mr. Keogh wrote. This would permit physicians and others to withdraw money from their pension plan prior to reaching age 65, subject to a penalty equal to the taxes previously deferred on the amount withdrawn.

Mr. Keogh said it was hoped that an amendment along this line "will dissipate any remaining substantial objections to the present form of the bill, especially those originating in insurance circles." He added: "The sponsors of the legislation, including all recognized national professional associations and many other self-employed groups . . . and those who will introduce the amended bill, hope that if you are a member of the next Congress, you will support the amended bill. We think that if you make known to those professional, agricultural and business groups in your district your support of the bill, it will not only be of considerable assistance in your reelection but will assure its passage next year." The American Medical Association has long advocated passage of legislation along these lines. Mr. Keogh reports that support for the idea is growing and that he is more optimistic of action next session than at any previous time.

PUBLIC HEALTH SERVICE PERSONNEL CHANGES

Major shifts in top personnel of the U. S. Public Health Service have been announced by Surgeon General Leroy E. Burney. They are the first since he took office last August from Dr. Leonard Scheele, who is now with a pharmaceutical firm. The reassignments involve four physicians, all career officers in the PHS. They become effective Nov. 1.

Dr. Jack Masur, an assistant surgeon general in charge of the Bureau of Medical Services, is shifted to the Clinical Center in the National Institutes of Health at Bethesda, Md. Before becoming chief of the bureau in 1951, Dr. Masur was in charge of planning and construction of the 500-bed center. He entered the PHS in 1943 after serving in administrative posts at Lebanon Hospital and Montefiore Hospital in New York City.

To fill Dr. Masur's post, Dr. John W. Cronin, head of the Hill-Burton hospital construction program for the past seven years, is being promoted. Dr. Cronin has been with the service from the time he was an intern in 1932 and has had postgraduate training in psychiatry. The bureau, one of the largest in the PHS, supervises all PHS hospitals, Indian health and foreign quarantine programs, the Hill-Burton program, and dental and nursing resources activities. Dr. Van M. Hoge, now associate chief of the Bureau of Medical Services, also takes over the Hill-Burton directorship. Dr. Hoge was the first director of the Hill-Burton program when it was launched 10 years ago. He continues his duties in the bureau under Dr. Cronin. Dr. D. W. Patrick, current director of the center, will be given a new assignment as yet undesignated.

The Burney announcement stressed the importance of the Clinical Center, which was described as the "largest facility of its kind in the world for research in the major diseases of today." Present facilities are about to be expanded to permit even greater research in neurological and cardiac surgery. Dr. Burney also

(Continued on page 22)

From the Washington Office of the American Medical Association.

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brand

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Dear Doctor:

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(cont'd) ↗

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Washington News—Continued

has asked Secretary Folsom of the Department of Health, Education, and Welfare to approve an upgrading of the directorship of the Clinical Center so that it requires the rank of brigadier general rather than colonel. Dr. Cronin, meanwhile, will be nominated as assistant surgeon general with the rank of major general, which is required for the chief of the Bureau of Medical Services.

FOREIGN SERVICE FOR PUBLIC HEALTH NURSES

The State Department has openings for public health nurses in "most parts of the world" in its Foreign Service. They will be assigned to embassies for their two-year tours of duty, and as far as possible their wishes will be observed as to the country in which they will serve. They must have a degree with a public health major and a year's experience in some generalized public health program. For information, contact Miss Evelyn E. Weigold, Nurse Consultant, Department of State, Washington 25, D. C.

VENEREAL DISEASE PROGRAM

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The medical section of the bulletin, revised by Dr. Marian M. Crane, chief of the research interpretation branch, discusses first the importance of regular examinations by the doctor. The mother can facilitate these examinations if she is prepared to answer questions on the child's eating, sleeping, and play habits. Another suggestion is to keep a record of your child's bruises, falls, and cuts.

The remaining part of the medical section is concerned with the prevention of disease. The bulletin lists the precautions necessary to avoid contracting such diseases as influenza, tuberculosis, dysentery, and roundworms. Good health routines, immunization plans, and sick room procedures are outlined carefully. In the final pages the symptoms and course of various childhood diseases are discussed. The bulletin is available from the Superintendent of Documents, Government Printing Office, Washington 25, D. C. It is priced at 20 cents a copy.

PERSONNEL

Brig. Gen. Wendell H. Duplantis is the new assistant administrator in charge of Operation Control Services, the nerve center of the Federal Civil Defense Administration. He retired from the Marine Corps last month after a career of 21 years. . . . James E. Webb is a new member of the National Advisory Cancer Council, which advises on research activities of Public Health Service's National Cancer Institute. . . . At the 63rd annual meeting of the Association of Military Surgeons medical awards will be presented to Col. Eugene C. Jacobs, Army; Capt. Robert S. Poos, Navy; Dr. George M. Lyon, Veterans Administration; Lieut. Col. Edwin J. Pulaski, Army; and Capt. Elinor Pearson, Army.

Familial Leptocytosis.—Familial leptocytosis, thalassemia, or Cooley's anemia is apparently an ancient disease. Anthropologic studies indicate it may have been present in Sicily in paleolithic times. However, it was first identified as a separate entity by Cooley and Lee in 1925 and again by Cooley, Witwer, and Lee in 1927. They described a series of cases of anemia with splenomegaly and peculiar bone changes occurring in children of Greek, Italian, Syrian, or Armenian descent. . . . A review of the existing Italian literature indicates the following pathogenesis of leptocytosis. A spontaneous mutation of the red cells occurred in the ancient race about the Mediterranean Sea, which inserted itself in the ethnic structures of some countries (mainly, Italy and Greece). The inherited defect consists of a morphologic alteration of the red blood corpuscles. The cell is formed with an adequate or excessive membrane, which contains little hemoglobin substance, so that the cell appears to be thinner (leptocyte) and of a smaller volume (microcyte) than the standard normal red blood corpuscle. As a result such a red blood corpuscle shows an increased resistance to hypotonic saline solution. It also possesses a life span of shorter duration than the normal cell which in vivo results in corpuscle losses. This condition causes a chronic stimulation of the bone marrow with medullary hyperplasia of the erythroblastic series. Immature cells showing stippling, polychromatophilia, and erythroblastosis appear in the blood. The bone marrow becomes hyperactive (erythroblastosis), and osteoporosis occurs (x-ray observation), as well as splenomegaly. Erythrocytes, together with leptocytes and microcytes, and the increased resistance to hypotonic saline solution make up the features of the peripheral blood picture.—P. R. Casesa, M.D., Familial Leptocytosis, *New York State Journal of Medicine*, May 15, 1956.

(cont'd)

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Washington News—Continued

has asked Secretary Folsom of the Department of Health, Education, and Welfare to approve an upgrading of the directorship of the Clinical Center so that it requires the rank of brigadier general rather than colonel. Dr. Cronin, meanwhile, will be nominated as assistant surgeon general with the rank of major general, which is required for the chief of the Bureau of Medical Services.

FOREIGN SERVICE FOR PUBLIC HEALTH NURSES

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THE JOURNAL

of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 162, NO. 10 CHICAGO, ILLINOIS NOVEMBER 3, 1956

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VISUAL INTRACARDIAC SURGERY IN A SERIES OF ONE HUNDRED ELEVEN PATIENTS

Henry Swan, M.D.
and
S. Gilbert Blount Jr., M.D., Denver

• *The use of general hypothermia in order to permit cardiac surgery to be performed on the open heart with a dry field under direct vision has intrinsic, unknown risks. These have been analyzed in 111 patients, the largest group being 58 patients with atrial septal defects. Of 19 fatalities, 8 were due to cardiac failure, 4 to thrombosis, 4 to hemorrhage, and 3 to other causes. The hazards both of the cardiac arrhythmias and of the disturbances of clotting can be greatly reduced by not exceeding a limit of eight minutes of circulatory occlusion, by not using this technique for procedures that cannot be readily accomplished within this time limit, and by keeping the temperature within the range from 29 to 32 C (84.2 to 89.2 F). Within these limitations, pulmonary valvular and infundibular stenosis, atrial septal defect, and aortic stenosis can be readily repaired at low risk. The risk is justified by the sometimes dramatic improvement seen after operation in patients with otherwise hopeless conditions.*

This report is concerned with an analysis of our clinical experience with one method (hypothermia) for achieving the major goal of cardiac surgery; namely, open heart, dry field, and direct vision. Deep is our conviction that from the surgical point of view increasing experience will enable most if not all current and future operative procedures within the heart to be accomplished with deliberation under these conditions. By one technique or another, the risk to the patient will be as low or lower and with better results than current blind manipulations guided only by the sense of feel. Surely the accuracy that vision gives to technique, together with the versatility it allows in coping with unexpected variants of the defect, will effect results that are superior from all standpoints. This is already true of valvular and infundibular pulmonary stenosis, atrial septal defect, and ventricular septal defect. We believe it will eventually be true of all intracardiac procedures.

In the exploration of any new technique, however, though the successes be gratifying, the way is strewn with occasional bitter defeats that seem doubly difficult to accept as one realizes that increasing knowledge and experience will probably prove that many such failures would later be preventable. Yet, thus it is with all clinical exploration of new horizons, and one seeks strength in the conviction that in each patient the diagnosis was as certain as possible, the need for surgery was definite and urgent, and the background of experiment was as broad as possible. Not all the questions, however, can be completely solved in the laboratory; in the end, clinical trial must be made and the vital human problems faced.

The operations performed in this series of patients were all done during general hypothermia. The methodology of our management of hypothermia has been described in previous publications,[1] and will not be elaborated here. Moreover, the actual operative techniques have also been described,[2] so these will not be further discussed. We are primarily concerned here with the results of the procedures. When one is utilizing a new modality such as hypothermia, with its intrinsic but unknown risks, and then superimposes in addition a new technical method, such as open suture closure of atrial septal defect, open pulmonary or aortic valvuloplasty, or suture closure of ventricular septal defect, one may have difficulty in assessing the reasons for success or failure in a single patient. We have attempted to evaluate our results in spite of the complexity of the variables.

From the departments of surgery and medicine, University of Colorado School of Medicine.

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postoperative physiological studies reveal that 15 of these 17 patients have achieved a cure, which we have arbitrarily defined as a postoperative residual systolic pressure gradient between the right ventricle and the pulmonary artery of 20 mm. Hg or less. In the 17 patients recatheterized, a systolic pressure gradient of less than 10 mm. Hg was noted in 9 patients and less than 20 mm. Hg in 6 patients. In the remaining two patients there were gradients of 26 and 28 mm. Hg. Diastolic pulmonary artery pressures have remained normal, and significant pulmonary regurgitation has not occurred in any patient. Although this series is still relatively small, it is our conviction that this current operative approach is a both safe and eminently effective one and is superior to the blind transventricular approach.

Infundibular pulmonary stenosis with an intact ventricular septum is a relatively rare congenital lesion. However, in this series such lesions have been evaluated in two patients, and resection of the infundibular stenosis performed. It is often difficult to be certain from the physiological studies as to whether the ventricular septum is intact, for oftentimes, although no shunt in either direction is definitely established, postmortem examination may reveal the presence of a small defect in the ventricular septum. However, when the stenosis is established as being in the infundibular area, there is no physiological evidence of either a left-to-right or right-to-left shunt at the ventricular level, and the right ventricle is hypertrophied with an elevated pressure, then surgery is definitely indicated. Since there is no defect in the ventricular septum, the surgeon can remove the area of infundibular stenosis completely without concern for the abrupt development of a significant left-to-right shunt after the removal of the infundibular stenosis.

Table 2.—*Results of Surgery in Patients with Atrial Septal Defects*

Disease	Patients, No.	Operations, No	Proved Total Cure	Improved	Unimproved	Dead	Too Recent to Evaluate
Atrial septal defect (secundum)	45	46	26	9	0	7	3
Atrial septal defect (primum)	1	1	0	1	0	0	0
Hiatus atrioventricularis communis	3	3	0	0	1	2	0
Atrial septal defect and pulmonary stenosis	9	10	1	4	0	2	2
Total	58	60	27	14	1	11	5

Table 3.—*Results of Surgery in All Patients with Pulmonary Stenosis*

Disease	Patients, No.	Operations, No.	Total Cure	Improved	Unimproved	Dead	Too Recent to Evaluate
Valvular stenosis	25	25	15	7	0	0	3
Infundibular stenosis	2	2	1	1	0	0	0
Trilogy	9	10	1	4	0	2	2
Tetralogy, infundibular	10	10	0	7	0	3	0
Tetralogy, valvular	7	7	0	7	0	0	0
Total	53	54	17	26	0	5	5

The two patients in this series considered to have had this anomaly have both had excellent results, and one is considered cured. Thus, in one patient the systolic pressure gradient between the right ventricle and pulmonary artery was completely abolished, and the postoperative studies revealed no evidence of a shunt in either direction. The remaining patient, completely asymptomatic, had a postoperative pressure gradient of 27 mm. Hg. Again, the currently suggested approach to this lesion is considered to be both safe and effective.

The indications for surgery in the patient with trilogy of Fallot are in general similar to those for valvular pulmonary stenosis with intact septums. Patients falling into this group usually, although by no means invariably, have a higher systolic pressure within the right ventricle, and, thus, almost always the indications for surgery are clear-cut. Early in our experience we had hoped that, with the regression of the right ventricular hypertrophy after valvuloplasty and the change in the pressure-volume relationship of this ventricle, the right atrial pressure would fall, the right-to-left shunt would be abolished, and possibly the foramen ovale might close, should that have been the defect in the septum. The follow-up course on some of these patients has not been sufficiently long as yet to prove or disprove this hypothesis. However, it would appear that in some of these patients the defect in the atrial septum will remain open and that a second operation for closure of the defect may be necessary, whether it be a dilated foramen ovale or a true atrial septal defect.

We have operated upon nine patients who fall into this category, with two deaths. One patient, 7 months of age, who had been very cyanotic, with a peripheral arterial saturation of 49%, died suddenly 14 hours after surgery. The operation and immediate postoperative course until time of death were uneventful. The other mortality was in a 19-year-old boy with a preoperative right ventricular systolic pressure of 175 mm. Hg and who was very cyanotic, with a peripheral arterial oxygen saturation of 74%. The valvular pulmonary stenosis was relieved without event; however, it was then decided to close the defect in the atrial septum, which was found by palpation to be of great size. The patient developed ventricular fibrillation before the atrium could be opened, and, although a normal sinus rhythm was finally established, the patient died six hours later. One patient on whom both pulmonary valvuloplasty and repair of atrial septal defect were done is now cured. The remaining four patients have all been greatly improved from the clinical viewpoint. Three have been catheterized postoperatively, one with complete obliteration of the preoperative right ventricle–pulmonary artery systolic pressure gradient. The remaining two had marked hypertrophy of the right ventricle and residual gradients of 33 and 31 mm. Hg.

The indications for resection of infundibular stenosis in the patient with a tetralogy of Fallot are less clear. However, in general, our experience has been that these patients are very significantly improved, and the improvement is certainly of an order equal to the anastomotic procedures of Blalock or Potts. However, the extent of the removal of the infundibular stenosis must be carefully judged, for, should the stenosed area be completely removed in the face of a large ventricular septal defect, dire consequences may result. With such complete relief of obstruction to outflow from the right ventricle, a large left-to-right shunt may be suddenly established, with resulting dilatation of the heart with myocardial failure or aneurysmal dilatation of the thin-walled infundibular chamber.[3] Thus, it is not considered wise to remove completely the stenosed area in these patients. Our results have in general been good with this procedure. The pulmonary artery pressure rises, and the pulmonary blood flow increases greatly. However, the right ventricular systolic pressure usually remains of the same order of magnitude as preoperatively. In general, then, removal of infundibular stenosis in the presence of a ventricular septal defect calls for partial excision. Total excision may result in great cardiac enlargement and congestive failure.

TABLE 4.—*Total Deaths in 111 Patients by Disease and Cause*

Disease	Hemorrhage	Postoperative Thrombosis	Cardiac Failure	Other
Atrial septal defect	1	4	2	
Hiatus atrioventricularis communis			2	
Trilogy	1			1 (Sudden death at 12 hr., cause undetermined)
Ventricular septal defect			4	
Tetralogy	1			2 (Transfusion anuria, death at 3 wk. of sepsis) (Postoperative aneurysm of right ventricle, died at attempted repair 3 mo. later)
Anomalous pulmonary veins	1			
Total	4	4	8	3

In 17 patients an open direct operative approach has been aimed at the pulmonary obstruction. Seven have had valvular obstruction and 10 infundibular. There have been no deaths in the first group and three in the second group. All patients have had marked improvement from the clinical standpoint, the cyanosis has disappeared or lessened to a striking degree, and their tolerance of exercise has been dramatically increased.

The patient with an atrial septal defect of the secundum type represents, in general, an ideal candidate for closure by direct vision during hypothermia. Although our criteria for operative intervention are still in the formative stage and will doubtless be altered as experience dictates, at the present time closure of a secundum type defect is being advised in all patients with a pulmonary index 2.5 times or more the systemic and in whom the total pulmonary vascular resistance is less than 350 dynes/seconds/cm.[5] Once again, there is no set figure for flow or resistance that can be considered as a rigid limit, and the over-all clinical evaluation of the patient remains of the utmost importance. However, it has been our experience that, in those patients with a pulmonary vascular resistance above 350 dynes, the risk of the operation has been great and the postoperative course has been complicated. Certainly, whenever possible, closure of the atrial septal defect should be urged and performed on children between the ages of 3 and 12 years, since, during this age period, the risk of the operation is least and the gain to be expected from operation is greatest. At the present time, 45 patients with atrial septal defects of the secundum type have been operated on, with 38 survivors. At surgery it was found that four of this number had, in addition, anomalous pulmonary venous connections to the right auricle or superior vena cava. In the last three of these patients, the defect was closed in such a way that drainage from these veins was into the left atrium at the completion of the closure.

Twenty-seven patients have been recatheterized following surgery, and it is considered that 26 have been cured, since complete obliteration of the previously existing shunt was demonstrated. In two patients there was a small residual left-to-right shunt. The first was the initial patient encountered with one pulmonary vein from the right lung entering the right atrium, and no attempt was made to alter the site of drainage when the atrial defect was closed. The remaining patient had a huge defect (7 cm. by 5 cm.), and, at that time, closure was being effected by interrupted sutures. It is assumed that a small opening between sutures has persisted. Clinically, however, this patient has experienced a very dramatic improvement. Currently, a continuous suture is used. This experience leads us to the conclusion that closure of atrial septal defect of the secundum type by this method is reasonably safe and is a curative procedure.

Our experience with a direct vision transaortic approach to aortic valvular stenosis is still limited. We believe that, even under conditions of direct vision, in the older age group when the aortic valve is markedly calcified and deformed, operative intervention offers relatively little except in rare instances. Ideal candidates are the young patients with congenital aortic valvular or subaortic stenosis or the patients below 40 years of age with acquired rheumatic disease but without evidence of calcification of the valve. To date, the open operation has been performed in three patients, one with rheumatic stenosis of the aortic valve and the remaining two with congenital aortic disease, valvular in one and subaortic in the other. There have been no deaths, and the operative and postoperative course has been uneventful. It is felt that the accuracy of the visual procedure will help prevent the production of aortic regurgitation, a lethal complication of the blind technique.

Cause of Deaths

An analysis of the cause of death in this series is illuminating and in a sense encouraging, since it seems likely that current techniques will afford considerable safeguard against at least two of the major causative factors. Table 4 records the deaths by cause. The cause of death was most frequently cardiac in nature—in four patients irreversible arrhythmia and in four others failure of the heart to tolerate the combined insult of a major operation and the attending manipulation, the hypoxia of circulatory arrest, and at times the additional trauma of resuscitation. These particular complications will be largely avoided by using our current temperature levels, since almost all fatal arrhythmias occurred below 28 C (82.4 F) or in connection with prolonged occlusion times.

The probable tolerance of the heart for surgery can largely be predicted. Therefore, the selection of patients for operation can greatly modify the over-all outcome in this regard. However, except in the face of circumstances that place the patient in a category that must be accepted as inoperable (for example, marked elevation of the total pulmonary vascular resistance or intractable cardiac failure), we will continue to offer operation to the desperately ill, even though it is realized by all concerned that there is a very significant operative risk involved. The risk without surgery in these patients, however, must be considered to be 100%.

The other major fatal complication was a disturbance in the clotting mechanism, either tendency to bleed excessively during surgery or intravascular thrombosis occurring in the postoperative period. These are both, in all probability, risks inherent to any operation during hypothermia. As regards the bleeding tendency, operation, hypothermia, and multiple blood transfusions are the ingredients, and each may play specific roles. A bleeding tendency (coagulation defect) in cyanotic cardiac patients undergoing surgery at normal temperature has been recognized.[4] Experimental alteration in the concentration of the formed elements of the blood and in the clotting mechanism during hypothermia has been widely noted.[5] The influence of multiple transfusions of stored blood on the bleeding diathesis is also well documented. Again however, current practice offers much hope that the incidence of this complication can be reduced. No patient whose body temperature was above 28.5 C (83.3 F) manifested this tendency to bleed excessively (coagulation defect). We believe the limitation of the degree of hypothermia to the 29 to 32 C (84.2 to 89.6 F) range, together with the use of fresh blood rather than stored bank blood, will essentially eliminate this problem.

Thrombosis

As regards thrombosis, the nature of the malformation itself may play a definite role, since it has occurred only in patients with atrial septal defects. In two patients with large shunts and massive enlargement of the pulmonary vascular bed, pulmonary venous thrombosis occurred, once on the fourth day and once on the eighth. We believe that the sudden reduction in the rate of pulmonary blood flow that occurs at the time of closure of the defect in these patients may set the stage for this complication. Currently, therefore, we are heparinizing postoperatively all adults with this disease. The other two episodes, one thrombosis of a cerebral artery on the second postoperative day and the other thrombosis of both jugular veins on the night of surgery, remain unexplained, although avoidance of any constriction in the neck during anesthesia is currently being emphasized. In general, it is believed that, by staying within our current limitations of the technique, one may expect a marked reduction in the occurrence of both cardiac arrhythmias and the disturbances of clotting mechanism.

Summary

In 111 patients who underwent open heart, dry field visual surgery during hypothermia, a large variety of congenital defects was repaired. We have come to believe that the optimal temperature level is the range of 29 to 32 C (84.2 to 89.6 F) and that avoidance of lower temperatures will largely eliminate two of the major complications, namely, cardiac arrhythmias and disturbances in the clotting mechanism. At this temperature, we believe that six minutes of circulatory occlusion is safe and eight should not be exceeded. Within these limitations, pulmonary valvular and infundibular stenosis, atrial septal defect, and aortic stenosis can be readily repaired at low risk. The eminently satisfactory results of open operation in these diseases make an eloquent plea for a broader adoption of open heart techniques.

Addendum

Since the time of this study, 19 additional patients have undergone operation without loss of life. Thus, at a temperature range of 30 to 32 C (86 to 89.6 F), there has been only one death in the last 30 patients undergoing open operation for pulmonary valvular stenosis, aortic valvular stenosis, or atrial septal defect. As currently employed, open operation during hypothermia for these conditions should present a risk of less than 5%.

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The experimental background of this clinical series was supported by grants-in-aid from the U. S. Public Health Service and the American Heart Association and by a contract with the Office of the Surgeon General, U. S. Army.

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CUTANEOUS SENSITIVITY REACTIONS TO CHLORPROMAZINE

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- *Eighty-five patients manifested skin eruptions while being treated with chlorpromazine. While 57 of these had generalized reactions, almost all types of cutaneous eruptions occurred, with the exception of mucous membrane involvement. Dosage in these cases averaged 400 mg. or more a day. The lesions disappeared when the dosage was decreased or discontinued.*

Patch tests indicate chlorpromazine to be a primary irritant when applied full strength and may be of little value in determining potential reactors to systemic administration of the drug.

Among the many new tranquilizing-type preparations that have become commercially available within the past few years, the one that seems to have gained the most widespread use is chlorpromazine. This preparation is not unlike other effective drugs, in that after its use certain side-reactions or idiosyncrasies may develop. Some of the untoward reactions or complications that have been reported are orthostatic hypotension, obstructive jaundice, Parkinsonism, toxic delirium, asthmatic attacks, agranulocytosis, and numerous forms of skin reaction.[1] Lewis[2] has dealt primarily with skin manifestations, and others have reported dermatitis as a side-reaction.[3] The purpose of this paper is to describe the various cutaneous reactions that may result from the administration of chlorpromazine. An effort will be made to evaluate the use of the patch test in determining the presence of factors of primary irritation and sensitization and the value of this test in predicting susceptibility.

Material and Method

Our series consists of 85 patients manifesting skin eruptions due to chlorpromazine. It does not include approximately 200 other patients who have been observed but on whom records were inadequate for purposes of this study. Fifty-seven patients presented some type of generalized reaction. This group can be subdivided according to the following reactions: erythematous morbilliform with edema, urticarious, seborrheic, purpuric, papular, bullous, and miliaria-like. In the group of 18 patients with cases characterized by photosensitivity, the majority of the lesions were of an erythematous papulovesicular type, with one a severe bullous eruption. These lesions appeared only at the sites that were exposed to sunlight and occurred predominantly during the extended summer season characteristic of this geographical area. In 10 cases attributable to contact with the drug, the lesions were found predominantly on the dorsa of the hands and flexors of the elbows, neck, and face. The reaction was a typical erythematous eczematous dermatitis, which one would expect with an allergenic contactant. The majority of the patients in this series were given patch tests with full-strength solutions (25 mg. of chlorpromazine per cubic centimeter) by the closed and the open methods. In addition, volunteers were given patch tests with various concentrations by open and closed methods in an attempt to determine the primary irritant quality of this preparation.

Results

As can be seen in the table, this preparation can produce almost every type of cutaneous reaction. It is interesting to note that no mucous membrane lesions were observed in any of the patients studied. Of the subjects having generalized cutaneous eruptions, 35 of the 47 were females. With the exception of two cases, skin reactions did not appear until the dosage reached 400-600 mg. of chlorpromazine per day. During the hot summer months many of these subjects demonstrated a sweat gland obstructive reaction in the form of a miliaria-like eruption. The majority of eruptions were of the miliaria crystallina type; however, some of them seemed to have deeper obstruction of the sweat pores. Patch tests applied to these individuals showed that the full-strength solution gave positive reactions, but in most instances they were of the delayed type. In view of these findings, patch testing would appear to be of relatively little value in determining whether chlorpromazine was the responsible agent. As is shown below, this conclusion was confirmed by results obtained from routine patch testing of volunteers.

Total daily dosage, which ranged from 50 mg. to 1.2 gm., played little part in the production of photosensitization reactions. The highest percentage of eruptions in this category were of the papulovesicular variety and occurred at the sites of exposure. One severe bul-

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Read before the Section on Dermatology at the 105th Annual Meeting of the American Medical Association, Chicago, June 12, 1956.

lous eruption appeared within two hours after a 20-minute exposure to sunshine. The lesions produced by photosensitization, with the exception of the single bullous reaction, were deep-seated, indicating that the site of disturbance was probably in the upper cutis. A considerable degree of brawny-type edema was associated with these lesions. It is well known that the wave lengths of summer sunlight differ from those of the winter.[4] Although this study was not specifically concerned with the effect of particular light wave lengths in the production of these dermatoses, the higher summer incidence is strongly suggestive that this difference may be a major factor.

The results of 48-hour patch tests utilizing the full-strength solution in 557 volunteers show: 79 individuals gave 1+ reactions, 36 showed 2+ reactions, 6 had 3+ reactions, and 2 gave 4+ reactions. There were 32 who gave a 1+ to 3+ reaction in a delayed manner, the reaction appearing about the fifth to seventh day. No reactions were observed in 402 subjects.

In an additional group of 845 individuals who had multiple test concentrations applied, some had three types of tests: full-strength closed, full-strength open, and 10% closed. In others, combinations of only two of these tests were used. A total of 114 had positive reactions. There were 101 positive reactions in 338 test subjects who received the full-strength closed patch test. Nine positive reactions were seen in 218 patients receiving the 10% closed patch test, and there were four positive reactions in the 289 individuals given the full-strength open test. In two instances paradoxical reactions occurred in which the individual reacted to the more dilute solution or open test but did not react to the full-strength closed test. This group also contained a number of subjects with delayed reactions.

Skin Reactions to Chlorpromazine from Systemic Use

Type Reactions	No of Cases	Dosage Range, Mg./Day	Mean Dosage, Mg./Day
Erythematous morbilliform	47	200-2,400	800
Photosensitization	18	50-1,200	200
Urticarious	7	200-1,200	500
Petechial	2	700	700
Bullous	1	400-800	600

Ten cases of contact dermatitis resulting from the subjects having worked with chlorpromazine were found. In a majority of instances the subjects were nurses or hospital employees who were required to handle this preparation as part of their duties. As would be expected, the principal sites of reaction were the dorsa of the hands and flexors of the arms, face, and neck. These lesions, which appeared from two to eight weeks after contact, were rather recalcitrant to the usual methods of therapy and resembled other types of allergic epidermal contact dermatitis. Although the degree of reaction varied with the concentration of the patch test, all these persons demonstrated flare-ups of their contact areas after the patch test procedure. Three of these patients showed a delayed type of reaction, particularly if their previous dermatitis had completely cleared. It was believed that the contact region was aggravated by sunlight, although at this time we do not have adequate statistics to support this finding. Some of the volunteers demonstrating delayed patch test reactions associated appearance of a reaction with exposure to sunshine.

Comment

There are many features about the cutaneous reactions to chlorpromazine that are a decided variation from those to other systemically given medicaments that produce skin reactions. First, the reactions produce a minimal amount of symptomatology as compared with other drug eruptions. Second, these reactions clear quite rapidly in a period of two to five days when therapy is discontinued. Once the dosage has been decreased or discontinued, the lesions disappear, and, in the majority of the cases studied, the preparation could be readministered with no recurrence. We attributed this to the fact that in none of these cases was the dosage returned to the previous high. There is a possibility that a form of desensitization has been produced, but this requires more study for corroboration. Cases in which dermatitides have cleared without interruption of therapy have been described.[5] Although there were purpuric and petechial eruptions in some instances, there was no alteration in the platelet count. In several of the cases we noted that the individuals predisposed to seborrhea had a decided flare of their seborrheic dermatitis. The fact that no mucous membrane lesions have been observed in these cases places this drug in a unique category.

We cannot account for the fact that we have seen no cutaneous reactions in the Negro race, but one could speculate that this is because of either the low case incidence in this series or better tolerance of sunlight. The generalized reactions have been much more frequent in women, but the cases of photosensitization are approximately equal in the two sexes. The contact-type dermatitis was also more prevalent in women, but this is probably occupational. Routine positive patch tests were found equally divided between men and women.

The rather marked number of reactions to the full-strength closed test puts this preparation into the primary irritant category. By the same token, the patch test method is precluded as an indicator of whether a prospective patient might react to this substance. It is thus similar to other drugs that give dermal reactions, in that the patch test is of little value in determining sensitivity. However, we feel that definite epidermal sensitization to this product does develop, as demonstrated by the cases of contact dermatitis. Due to the marked flares of the involved areas when the full-strength patch test was utilized, it is felt that a 10% concentration with the closed patch test or the open drop method should be used when testing for sensitivity. The mild sweat retention syndrome that was demonstrated in a number of cases is attributed to the inflammatory action manifested in the regions of the lower epidermis or upper dermis.

Summary and Conclusions

Eighty-five persons tested had various types of reactions to chlorpromazine. In the majority, patch tests, as well as results obtained from testing several hundred volunteers, revealed that this substance is a primary irritant when applied at full strength. This suggests that patch tests are of little value in determining whether a patient might react to chlorpromazine given systemically. It is suggested that a 10% solution in a closed patch test or full-strength open tests be utilized when attempting to determine contact sensitization reactions. There is probably a critical dosage level that is necessary to produce a reaction in the majority of cases. In this study the range was above 400 mg. of chlorpromazine per day and in most instances was near 600 mg. per day. It is thought that the dosage level plays no role in the production of a photosensitization reaction. Almost all types of cutaneous reactions have been induced by chlorpromazine, with the exception of mucous membrane lesions. The skin reactions following systemic administration of this drug clear r[illegible] the dosage is decreased or discontinued, whereas contact dermatitis is usually severe and recalcitrant to therapy.

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PRELIMINARY OBSERVATIONS ON USE OF FRENQUEL IN HOSPITAL PSYCHIATRY

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• *The effects of Frenquel were studied in 100 psychotic patients. Symptoms proved to be more useful than etiology in classifying the results, and many disturbed patients were quieted regardless of the accepted diagnosis. Improvement, if it occurred, was unequivocal and convincing. Twenty-two of the psychotic patients, for instance, were classified as subacutely disturbed, and 13 of these were definitely improved. Among 20 psychotic patients with subacute conditions classified as quiet, however, there was improvement only in six. The highest percentage of successes was among 11 acutely psychotic patients, 8 of whom were definitely improved. Many of the patients received 100 mg. of the drug intravenously in the beginning and continued receiving from 80 to 180 mg. daily in divided doses by mouth, but as a rule the dosage was 40 mg. by mouth four times a day. Six case histories are given to illustrate the uses of Frenquel. It did not manifest specific antihallucinatory properties, did not produce the immobilization that can be obtained with chlorpromazine or reserpine, and did not afford good control of anxiety in the nonpsychotic patient. Its greatest value was in controlling the hyperactive, acutely disturbed patients whose usual emotional defenses are in process of breaking down. In such patients it can be used over longer periods of time, for it proved to be singularly free from side-effects.*

Our interest in Frenquel [α-(4-piperidyl) benzhydrol hydrochloride] was stimulated in part by earlier studies with pipradrol (Meratran) hydrochloride, an antidepressant and antifatigue compound, and in part by the work of Fabing,[1] who reversed, with intravenous administration of Frenquel, the hallucinations and perceptual and emotional distortions produced in normal subjects by lysergic acid diethylamide (LSD-25). The published reports of clinical experiences are incomplete at this time.[2] From impressions derived from the study of 100 cases, however, an attempt has been made to answer five questions: 1. What are the indications for the use of Frenquel? 2. Does it possess a specific antihallucinatory effect? 3. How do the results of Frenquel therapy compare with those of reserpine and chlorpromazine hydrochloride? 4. Is Frenquel synergistic with the other tranquilizing drugs? 5. Are there any side-effects in therapeutic dosage levels?

Indications for Use

The indications for the administration of Frenquel seem to depend not on the clinical diagnosis but rather on the patient's behavioral pattern and the course of the illness. In general, indications for the use of this drug are (1) an acute psychotic reaction and (2) an increase in psychotic manifestations, such as disorientation, confusion, delusions, hallucinations, or hyperactivity. The following conditions are worthwhile indications for a trial of Frenquel: acute schizophrenic reactions or exacerbations of a chronic schizophrenic process, acute manias, and delirious

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Read before the Section on Nervous and Mental Diseases at the 105th Annual Meeting of the American Medical Association, Chicago, June 12, 1956.

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mias due to endogenous or exogenous toxins. The table summarizes the results of Frenquel therapy in 100 psychotic patients. In evaluating improvement, it appeared more significant to classify the patient by the terms "quiet" or "disturbed" rather than by etiological diagnosis. Of this group, two-thirds were schizophrenic; patients with manic-depressive psychosis, toxic psychosis, and cerebral arteriosclerosis made up the rest. Disturbed behavior and the acuteness of the illness appeared to be prognostically positive factors. Psychiatric rating scales were not used, because we were interested in more than subtle behavioral changes. Where definite improvement is recorded, either the patient's condition went into a complete remission or the psychotic process was unequivocally improved.

Anxiety in the nonpsychotic patient is not well controlled with Frenquel. Eighteen patients with severe anxiety symptoms due to acute myocardial infarction were given a course of this drug. Two of the 18 developed toxic psychosis complicating their serious cardiac disease. While taking Frenquel, their confusion, disorientation, and panic-like state abated; but, when they were given placebos, their disturbed condition recurred, being brought under control again with the resumption of use of Frenquel. The remaining 16 showed no definite response to the drug. We inferred from this experience that Frenquel cannot be expected to modify anxiety in the nonpsychotic individual. However, it was gratifying to find a drug without hypotensive properties that could be used to reverse the psychotic delirium that is seen sporadically after a myocardial infarction.

TABLE 1.—*Evaluation of Improvement in Patients on Frenquel Therapy*

Condition and Classification	Definite	Slight or Questionable	No Change
Acute	8	3	...
Subacute			
Quiet	6	6	8
Disturbed	13	2	7
Chronic			
Quiet	...	6	24
Disturbed	6	5	6

Antihallucinatory Activity

Since hallucinations and perceptual and emotional distortions produced by lysergic acid diethylamide had been reversed by Frenquel,[2] it was anticipated that Frenquel might have a specific antihallucinatory activity. Our findings do not support this assumption. Although some patients lost their hallucinations, and many became less disturbed by them as their mental disorder ameliorated, there seemed to be no preferential reduction of the hallucinatory segment of their illness. Hallucinatory and delusional perceptions would seem to be projections of psychotic anxiety and are attenuated by a reduction of the anxiety. To test the premise that Frenquel is not solely an antihallucinatory agent, the 30 "quiet" patients with chronic hallucinations reported in the table were selected for treatment. No material subjective changes were observed. On the other hand, the six "disturbed" patients with chronic schizophrenia (see table) who showed definite improvement in their total clinical picture also ceased reacting to their hallucinations.

Comparative Results and Combined Therapy

Twenty-seven patients had been given prior courses of electroconvulsive therapy, reserpine, or chlorpromazine. In general, these were schizophrenic patients who had done poorly under the electroconvulsive treatments or who had improved initially but later become worse. The majority also had had previous treatment with reserpine or chlorpromazine and had shown variable degrees of improvement while receiving these drugs, but they had had exacerbations when the drugs were withdrawn. These patients were given Frenquel in order to compare its effect with those of the other forms of treatment. It was found to be a satisfactory tranquilizing agent, but, just as with other ataraxics, there were treatment failures. Some patients were improved with use of all three drugs; others responded to only one of them. All the tranquilizing agents give satisfactory results in those psychotic patients with a recent onset or intensification of anxiety or hyperactivity. However, even in this prognostically favorable group there are treatment failures. In an attempt to explain this situation, Sarwer-Foner and Ogle[3] point out that, in the patient whose hyperactivity is, in itself, a defense or who equates passivity with femininity, extreme and antitherapeutic anxiety may develop with the administration of the tranquilizing drugs. We have seen this paradoxical response in a few patients with character disorders.

Within the limits of the specific indications, Frenquel seems to be comparable to reserpine and chlorpromazine in ataraxic effect, that is, in its ability to diminish mental confusion. However, it does not possess the immobilizing action of these agents. Under immobilization we include the loss of spontaneity, muscle weakness, and sedation that both reserpine and chlorpromazine can produce. In certain situations it is desirable to immobilize the patient; for example, when he is dangerously disturbed. Some of the best therapeutic results attributed to chlorpromazine and reserpine have been due not to their ataraxic effect but to their ability to immobilize otherwise unmanageable patients. Nevertheless, in some cases, immobility is undesirable and may represent a toxic action of the drug.

A small number of schizophrenic patients who had not improved on therapy with one tranquilizing agent were treated with a Frenquel-reserpine or a Frenquel-chlorpromazine combination. This combined therapy has produced responses that could not be achieved by giving a single drug. Since the precise mechanism of action of these agents is still unknown, it is impossible to explain why treatment with more than one compound should have real advantages. Reserpine may be involved in release of serotonin[4]; and chlorpromazine seems to produce changes in enzymatic activity, especially phosphorylation, in certain areas of the brain.[5] Because Frenquel is sometimes effective when other tranquilizers fail and is ineffective in some instances when the others are helpful, we have assumed that it acts on other neurochemical substrates.

Dosage and Side-Effects

Many of our patients were given 100 mg. of Frenquel intravenously at the institution of treatment and continued receiving orally amounts varying from 80 to 180 mg. daily in divided doses. As a rule, 40 mg. four times a day was ordered. When it was apparent that the drug produced no side-effects whatsoever in these amounts, an attempt was made to determine whether massive doses would improve the therapeutic results. Ten of the patients whose condition had changed only slightly on administration of 160 mg. daily were given 1,200 mg. daily for three weeks. On this regimen they showed no further improvement, but it was impressive to note that no side-effects or measurable disturbances of renal or hepatic function were detected.

An unsuccessful effort was made to uncover complications due to Frenquel therapy in our patients. No hypotensive reactions occurred. Psychotic patients with hypertension showed no drop in blood pressure as they had with reserpine. One patient commented on an unpleasant taste in his mouth while taking Frenquel. With proper indications, Frenquel may be the drug of choice because of its lack of adverse side-effects and its rapid action. Often the patient's response to the first intravenous injection will apprise the physician as to whether the patient will respond to Frenquel therapy. The drug should be withdrawn or another added if, after a few days' treatment, no beneficial effects are observed.

Report of Cases

CASE 1.—A 45-year-old man who had had no previous overt emotional difficulties sustained an acute coronary thrombosis just before admission to the hospital. His mother and father had died suddenly of heart attacks a few years previously, and three months before his illness his wife had deserted him. Shortly after his admission the thrombosis extended, leaving him seriously ill. He had frequent hallucinatory episodes and uncontrollable crying spells. Meperidine (Demerol) hydrochloride, and reserpine, 0.5 mg. daily, did not control his panic-like emotional state. Since the patient's blood pressure readings were at hypotensive levels, the physician did not desire to increase the dosage of reserpine. Immediately after Frenquel therapy was begun, the patient was more cheerful. His weeping became infrequent, and the hallucinations did not recur. Use of all sedatives and narcotics could be discontinued. Thus, where small amounts of reserpine had been ineffective, an excellent result was obtained with Frenquel in this patient with an acute psychotic reaction.

CASE 2.—A 39-year-old patient had been hospitalized for 11 years because of physical and verbal assaultiveness, alternating with periods of complete negativism and mutism. Several courses of electroconvulsive therapy during this time had been without benefit. A lobotomy one year previous to our study quieted the patient somewhat, but he still required almost continuous restraint and was periodically destructive or withdrawn. His auditory hallucinations were especially bothersome to him. While receiving 400 mg. of chlorpromazine daily, he seemed somewhat more relaxed and stopped breaking windows. Frenquel, 80 mg. daily for three weeks, was substituted, with the patient showing marked reduction of hyperactivity and aggressiveness. Then chlorpromazine, 1,600 mg. daily, was given instead of Frenquel; the patient became agitated, requiring frequent neutral packs and restraints. When Frenquel therapy was resumed, the patient quickly showed an excellent response and no longer needed restraints or hydrotherapy. He still occasionally paces the floor and gnashes his teeth, but he claims that he is no longer troubled by hallucinations. He has recently gone on his first furlough from the hospital in 11 years. He has been on maintenance therapy with 80 mg. of Frenquel daily for the past six months without relapsing to his previous destructive behavior. Thus, Frenquel was better than chlorpromazine in handling this difficult patient.

CASE 3.—A 57-year-old patient with hebephrenic schizophrenia, whose illness has extended over the past 20 years, was given reserpine, 6 mg. daily, to control his destructive, assaultive behavior. The therapeutic result was satisfactory. However, when reserpine therapy was discontinued, his hyperactivity recurred. Upon receiving 160 mg. of Frenquel, he showed the same measure of improvement that had been noted with reserpine. In this case, then, Frenquel was as effective as reserpine.

CASE 4.—A 25-year-old patient with paranoid schizophrenia had been hospitalized for 10 months because of assaultive and suicidal behavior, apparently in response to visual and auditory hallucinations. His ward physician summarized his treatment as follows: 160 mg. of Frenquel produced the same tranquilizing action as 16 mg. of reserpine and was more effective than 1,400 mg. of chlorpromazine daily. He stated further that Frenquel had no detectable effect upon the patient's hallucinations.

CASE 5.—A 64-year-old patient had been hospitalized for four years with a condition diagnosed as chronic brain injury due to alcoholism. He was restless, confused, and disturbed. When he was given 2 mg. of reserpine, his behavior was gratifyingly improved. After reserpine therapy was discontinued because it caused excessive drowsiness, the patient gradually relapsed. Frenquel therapy was started, with the result that his behavior again improved and he was no longer "dopey" as he had been while receiving reserpine. On this regimen, the former good result of reserpine therapy was regained and the undesirable side-effect was eliminated. Thus, Frenquel alone was able to control the psychomotor overactivity, and the grogginess that accompanied reserpine therapy could be avoided.

CASE 6.—Although this psychotic patient with cerebral arteriosclerosis was 89 years old, he represented a real problem in management because of his assaultiveness. He would attack attendants and other patients in response to delusions and had to be kept in restraints or oversedated with barbiturates. Chlorpromazine produced syncopal attacks, and reserpine was ineffective in controlling his condition. Therapy with Frenquel in 160-mg. daily doses resulted in a marked decrease in his assaultiveness. Each time the use of Frenquel was discontinued, to determine whether it was actually the effective agent, the nurses would protest to the ward physician. All observers are now agreed that the quieting effect noted while the patient was receiving Frenquel was not fortuitous. Frenquel was the agent of choice in this management problem.

Conclusions

Frenquel [α(4-piperidyl) benzhydrol hydrochloride] is of value in the hyperactive, acutely disturbed psychotic patient whose usual emotional defenses are in the process of breaking down. In the functional psychoses, a specific antihallucinatory property was not demonstrated. Frenquel does have effective ataraxic properties, although it will not produce the immobilization that chlorpromazine or reserpine can accomplish. The effects produced by Frenquel when combined with reserpine and chlorpromazine are encouraging and should be studied further. Since Frenquel is singularly without side-effects, it is the drug of choice when the other ataraxics produce undesirable reactions.

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TREATMENT OF LABIAL ADHESIONS IN CHILDREN

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• *Labial adhesions, in which the opposing epithelial surfaces of the labia minora stick together without any union of the deeper tissues, were observed in a number of young patients over a period of five years. Three cases are cited to show how these adhesions appear and disappear irregularly. At times it is easy to separate them; at other times it is painful. They are likely to recur when separated, but tend to disappear with maturity. When they cause symptoms such as dysuria, they should be separted. If they do not cause symptoms they should not be treated, but they should be brought to the attention of the parents and their generally harmless nature should be explained.*

Anyone who examines a large number of children and includes as part of his routine examination an inspection of the external genitalia will commonly find the labia minora fused together in the midline in the female infant and child. Even though the condition is a common one, there has been relatively little written on the matter. The purpose of this paper is to suggest that these adhesions be treated in a manner different from that recommended in what few articles have been written on the subject. Vulvar synechias, vulvar fusion, gynatresia, and coalescence of the labia minora are other names that have been given to these adhesions. However, since it is only the labia minora that are involved and since there is no true tissue union between the two labia but only a sticking together of the epithelial surfaces, the name labial adhesions seems adequate and will, therefore, be used in this paper.

No doubt many of the older doctors were aware of these adhesions and their nature, but it was not until 1936 that the first report appeared in American literature. This was by Nowlin and Adams,[1] who presented eight cases. A second article, published in 1949 by Nowlin and co-workers,[2] reported that they could find the reports of only 29 cases in American literature. However, they stated that the foreign literature was quite extensive. A clue to the actual frequency of these adhesions can be obtained from an article that was written by Bowles and Childs[3] and appeared in 1943. These latter two doctors tabulated 20 cases seen in their practices in less than one year. It is probable that the experience of these latter two reporters has been similar to that of most pediatricians, who have assumed that everybody else was aware of the frequency of these adhesions and so there was no use in writing about them. Thus it can be seen that, reading the literature, one gets an entirely erroneous concept as to the frequency of the condition. However, if one is not aware of the nature of this condition when first confronted with it, he is apt to make the mistake of believing the child has a serious congenital deformity. There are, in the few articles written, a number of instances cited in which this interpretation of the nature of these adhesions has caused unnecessary alarm on the part of the parents of the child.

Acquiring of Adhesions

In the earliest reports on this condition, it was assumed that the adhesions were congenital because they were present when the child was first examined, and the assumption was made that they had always been there. Thus, in 1940, Campbell[4] postulated an embryologic explanation that there was a midline fusion of the labioscrotal folds similar to the fusion that develops in the male but lacking the density of scrotal fusion. However, the large number of routine physical examinations that have been done on children in recent years have revealed adhesions in patients free from them in previous examinations, thus proving that the adhesions were actually acquired. Bowles and Childs,[3] in their report on 20 cases, stated that in one patient the fusion was definitely present at birth but that in all of their other patients it was noticed first in later infancy. Since the majority had had previous examinations, they were thus known to have acquired the condition. The one case observed at birth is unique, so far as I know. Its uniqueness is better realized when one considers that, as shall be seen later, these adhesions tend to disappear as the genitalia attain their adult characteristics. Then, when one remembers that the female newborn infant's genitalia temporarily have many characteristics of the adult's due to a leakage of some of the mother's female hormones into the baby's circulation, it can be understood why these adhesions are seldom seen in the newborn infant.

When it was realized that the adhesions were acquired, then, naturally, came the question as to why these children acquired them. The most commonly stated explanation for the appearance of the adhesions has been that they follow an inflammatory process in the vulva, at which time the edges of the labia are denuded and are then able to adhere one to the other. This has not been a satisfactory explanation of the cause. Many children who are more or less poorly cared for have some irritation of the vulva but no adhesions. On the other hand, children who are well cared for and are at all times free of any inflammation in this area commonly have adhesions. My experience has been that certain children tend to form adhesions for no apparent reason. By this I mean that the girls in whom these adhesions are present are, as a group, no different in their anatomy or in any other way from any other group of girls, insofar as I have been able to discern. Also, it has been observed that, when the adhesions are separated, they will often recur; and they recur repeatedly unless the mother is instructed to make almost a daily inspection to keep them separated. A possible explanation for the presence and recurrence of these adhesions is that the mucus secretions in such girls contain a certain peculiar musilaginous property that causes these two opposing surfaces to adhere, while, in girls with a more fluid type of mucus secretion, there is no tendency for adhesions to develop.

Lack of Symptoms

There are ordinarily no symptoms resulting from the presence of these adhesions. Other writers have noted this also. However, there is an occasional case of a child who does have some trouble. I have seen four cases in which a child was complaining of mild dysuria, which was, in each case, relieved by separating labial adhesions. Some writers have suggested that the adhesions might lead to urinary tract infection and be conducive to masturbation, but there are no well-documented instances in which this has been true. Barysh[5] mentions a patient who had enuresis in whom he found these adhesions; though there was no recurrence of the adhesions after he separated them, the enuresis persisted. Thus it would seem logical to assume that the adhesions were not the cause of the enuresis.

If it is agreed that the adhesions cause little trouble in the child, another question is: How does their presence affect the adult female? The answer is that, with maturity, the adhesions dissolve and disappear spontaneously. One must draw this conclusion, because, whereas the condition is known to be common in children, it is questionable that it is ever found in the adult. Campbell[6] reports having found firm adhesions with a tiny labial orifice in a 69-year-old female, and Taylor,[6A] in 1941, reported a case in a woman 74 years of age. If these were first observed at this age, one would wonder if they had not been acquired in later life in a manner similar to that in which the infant or small child acquires her adhesions. This would seem logical when one remembers that, in the elderly female, the genitalia atrophy and undergo changes so that they come to resemble the child's genitalia.[7] The fact is that adhesions in normal young and middle-aged adult women have not been reported.

Campbell[4] says that urinary disturbances could occur in children with marked labial fusion, and, as puberty is reached, the menstrual flow could be retained by the minute orifice, causing its collection in the vagina. However, none of his patients had menstruated, and he does not document any cases in which there were any of these complaints. In a similar vein, Bowles and Childs,[3] in their article on the subject, maintain that failure to eliminate labial synechias may occasionally be the cause of serious urinary and menstrual dysfunction or may prevent normal sex life. They do not, however, document any cases in which this has been true.

Treatment

In regard to treatment, all of the authors reviewed gave more or less the same advice, namely, that the adhesions be separated at the time they are discovered, regardless of whether or not the patient is having any symptoms due to the adhesions. It is recommended that an anesthetic be used, if necessary, while the adhesions are being separated. Then it is recommended that the raw labial edges be kept separated for some days while they are healing. This can be done with bland ointment or petrolatum or a pledget of cotton kept inserted between the labia until healing has been completed. Mothers are further advised to make frequent inspections thereafter and for an indefinite period of time to prevent recurrent adhesions. Since this latter instruction is commonly given, it is apparent that others have had experience similar to mine, namely, that adhesions tend to recur in certain children.

Prior to five years ago, it was my practice to separate the labial adhesions assiduously, as is common practice with most other practitioners. It was observed that the adhesions were reappearing, and separation was repeatedly being done on the same children.

There can be no question that separating of the adhesions is painful to the child, the degree of the pain depending somewhat on how firm the adhesions are. After separating the adhesions, one will observe that there is a red raw line on the edge of each labium where the adhesion has been broken. These raw edges, however, do not bleed. It was my practice to instruct the mother to put petrolatum on these edges until they had healed, but it was never my practice to instruct the mother to make a daily inspection of the child's genitalia for an indefinite period of time. Too-frequent attention to the child's genitalia is not advantageous, from a psychological point of view, if for no other reason. On several occasions the mother reported that the child had painful urination for 24 hours after the separation of these adhesions. This is easy to understand, since the passage of urine over the raw surface created by the operation no doubt would be painful. If the mother reported at the time the child was having trouble, she was advised to have the child urinate in a warm bath and thus gain relief.

For approximately the past five years, it has been my practice, whenever adhesions have been found on routine examination, to leave them entirely alone. However, at the time they are observed, they are pointed out to the mother and their presence described to her. At the same time she is told that this finding is purely incidental, that the adhesions are obviously causing no trouble, and that with maturity, or perhaps sooner, they will disappear. She is also told that it has been my experience that they seldom cause trouble and that if they are separated, they will probably recur. She is reassured that, if they do cause trouble, the trouble will probably be discomfort with urination and that the discomfort can easily be cured by separating the adhesions at the time the child is having the trouble. This treatment plan, which might be called the "no treatment plan," has been entirely satisfactory, and in every case the above explanation, when given, has been satisfactory to the mother also.

Report of Cases

CASE 1.—On routine examination of a girl who was first seen when she was 8 years old, firm labial adhesions were found. When their presence was pointed out to the mother, she stated that they had been present at every examination that the child had had since infancy and that at each examination the pediatrician had separated the adhesions. When an effort was made to separate the adhesions in the usual manner, it was soon apparent that the child was going to give a considerable amount of resistance and would certainly require an anesthetic. Since the adhesions were causing the child no trouble, it was agreed that they would simply be watched. One year later, when the child was 9 years old, the adhesions had partially disappeared and there was a good-sized opening between the anterior half of the labia. Again, when the child was 10 years of age, the adhesions were complete and firm. Two months after this examination, the child came in with the symptoms of frequency of urination and dysuria of two days' duration. The urine was clear, but she had firm, complete adhesions. The child permitted their separation without anesthesia, and there was immediate relief of symptoms. One year later, when the child was 11, the adhesions were again present and the child permitted their separation. Since this last examination the child has been followed by an internist, and there has been no further recurrence of the adhesions.

Case 2.—A child was seen at birth, at one month, and at 2 months, with no adhesions. At the 4-month and 6-month examinations, adhesions were present and were broken. At 9 months, there were no adhesions present. At one year, adhesions were present and were broken. At one and one-half years, adhesions were present and broken. There is no note on this subject from the 2-year examination. At the 3½-year and 4½-year examinations, adhesions were present and were left unbroken. At the 6-year examination, very firm adhesions were present with no opening seen, but they were left unbroken. At the 7-year examination, no adhesions were present. From age 2 on, each annual examination included a urine examination, which was always negative.

Case 3.—The younger sister of the patient in case 2 was seen at birth, one month, and 2 months with no adhesions present. At the 4-month examination, adhesions were present and were left unbroken. There is no note on this subject from the 6-month, 9-month, and one-year examinations. At the 18-month examination, adhesions were present and were left unbroken. At the 2-year, 3-year, and 4-year examinations, adhesions were present and left unbroken. At the 5-year and 6-year examinations, no adhesions were present. From 2 years of age on the child had yearly urine examinations, all of which were negative.

Conclusions

Labial adhesions are common in certain children, possibly due to some peculiar tenaciousness of the mucus secretions on the surfaces of the labia. Every doctor should recognize these adhesions in order to avoid causing alarm to parents. These adhesions seldom cause any trouble, but, if symptoms should develop that can be blamed on the presence of the adhesions, the labia should be separated at that time. Since these adhesions do cause little trouble and their removal is painful, and since they tend to recur and do tend to disappear with maturity, in most cases a "no treatment plan" should be tried.

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GRANULOMAS OF THE AXILLAS CAUSED BY DEODORANTS

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• *A new clinical entity, in the form of a previously unseen skin eruption, appears to be developing from the use of certain deodorant and antiperspirant preparations. While the clinical appearance and pathological examinations are consistent in all patients observed to this time, the exact etiology of the granulomatous lesion is still to be determined. This chronic condition, while evidently resistant to treatment, in the acute stage may be somewhat alleviated by topically administered steroids.*

A few months ago we submitted to The Journal a preliminary report on four cases of unusual eruption in the axillas after use of certain deodorants.[1] Since these cases are occurring more frequently, we are prompted to submit a more detailed clinical report so these cases may be more easily recognized. The original cases were all quite characteristically alike clinically and on histopathological examination and different from previously described eruptions in the axillas. All followed the use of a deodorant for a period of a few days to several months.

Report of Cases

Case 1.—A 37-year-old female office worker in December, 1955, developed an eruption in both axillas consisting of dusky reddish-brown papules that measured 1 to 4 mm. in diameter. These were very closely set in the domes of the axillas, but were more discrete at the periphery. Some of the lesions resembled vesicles, but yielded no fluid when punctured. Itching was mild. During the following six months the lesions flattened slowly, but considerable hyperpigmentation remained. Daily applications of stick deodorant had been used for two weeks prior to appearance of the eruption.

Histological sections, stained with hematoxylin and eosin, were prepared from a biopsy specimen of a typical papule in the left axilla. Upon first examination with the low-power lens, dense granulomatous infiltrate was seen, involving practically the entire corium. The infiltrate consisted of numerous epithelioid cells and giant cells closely packed together to form a tuberculoid pattern (fig. 1). Lymphocytes were present, but were not as numerous as expected. Most of the giant cells resembled the Langhans' type, as seen in tuberculosis, but some had the appearance of foreign body giant cells. There was no sharp circumscription of the tubercles that is so characteristic of sarcoidosis or sarcoid reaction. Necrosis was absent. The epidermis had lost its rete-peg structure and appeared thin, probably due to the pressure of the infiltrate from below. Polaroscopic examination of the same sections did not reveal foreign bodies.

Case 2.—A 30-year-old housewife suddenly developed a papular eruption in each axilla in January, 1956. For one month previously she had used daily applications of a stick deodorant.

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When first seen three months after onset of the eruption, she had numerous flesh-colored, smooth-surfaced, semiglobular, semitranslucent, discrete papules 1 to 4 mm. in diameter, which at first glance resembled vesicles. A few of the lesions were arranged in lines. Itching was minimal. Previous treatment with superficial x-ray therapy and hydrocortisone ointment had improved the condition only slightly.

Examination of histological sections stained with hematoxylin and eosin, from a biopsy specimen of a papule in the axilla, revealed a tuberculoid granuloma in the corium. The granuloma consisted of epithelioid cells and Langhans' giant cells surrounded by lymphocytes, to form the characteristic tuberculoid pattern (fig. 2). Necrosis was not discernible, and numerous small blood vessels were included in the granulomatous mass. Again the sharp delineation of tubercles necessary for a diagnosis of sarcoidosis was absent. The infiltrate followed along the course of vessels downward into the corium. Polaroscopic examination for foreign bodies was negative.

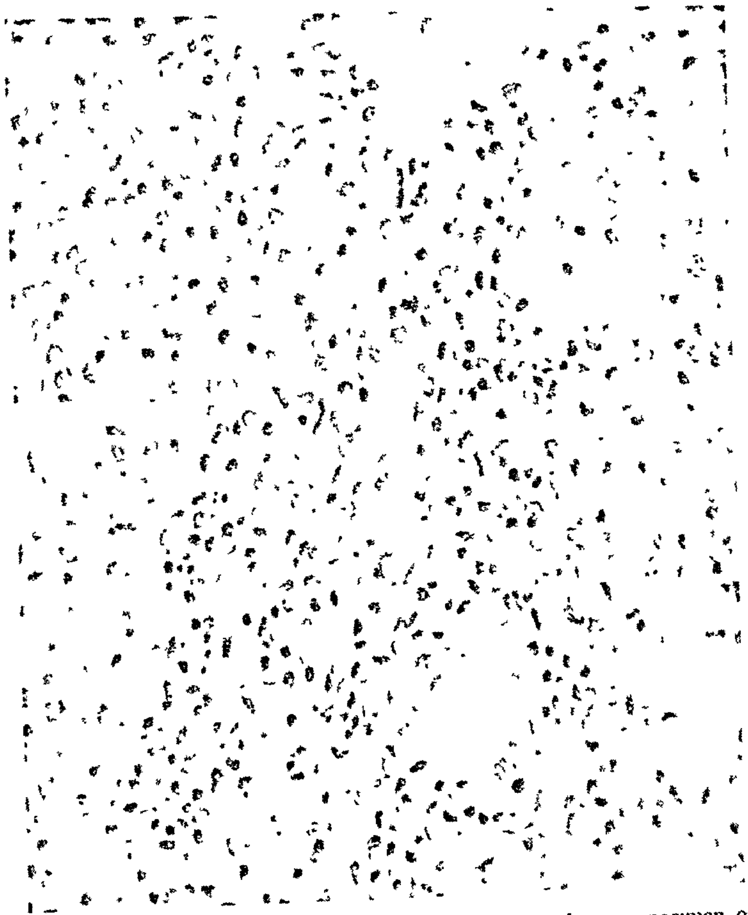

Fig. 1.—Photomicrograph of section prepared from biopsy specimen of typical papule in left axilla of patient in case 1.

Case 3.—A 56-year-old female stated she applied a stick deodorant to each axilla on March 17, 1956. The following morning the axillas were shaved. Two days later a moderately pruritic eruption appeared. When she was first examined five weeks later, there were innumerable dull, brownish-red pinhead-to-matchhead-sized papules in both axillas (fig. 3). Many of the papules were shiny and somewhat translucent. Pricking of the lesions did not reveal fluid. On diascopic pressure, "apple jelly" color was noted. After five weekly treatments with superficial x-ray therapy and application of hydrocortisone in lotion and cream form, there was little change except for a somewhat more yellow color and slight scaling. Intradermally given purified protein derivative of tuberculin, first strength, gave a negative reaction; the second strength showed a faint split-pea-sized reddish papule.

Sections stained with hematoxylin and eosin showed the essential pathology in the upper corium. A fairly dense granulomatous mass consisting of epithelioid cells, Langhans' giant cells, lymphocytes, and an occasional eosinophil surrounded a hair follicle (fig. 4). Many small blood vessels were included within the granulomatous area. Again polaroscopic examination did not reveal foreign material.

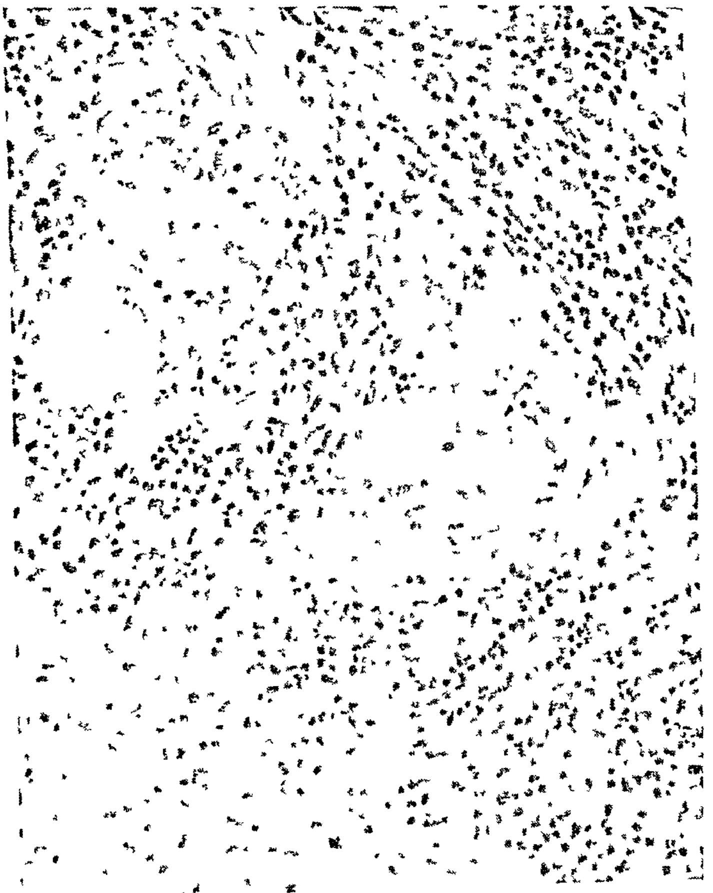

Fig. 2.—Photomicrograph of section prepared from biopsy specimen of papule in axilla of patient in case 2.

Case 4.—A 31-year-old female schoolteacher stated that two days after applying a deodorant lotion she noted burning and itching of the axillas. She had applied the lotion in the morning and had shaved the axillas that night. When examined 10 days later, both axillas were studded with BB-sized (about 2 mm. in diameter), dull, reddish-brown discrete papules. The lesions appeared glossy, with an occasional overlying telangiectatic vessel. Microscpoic examination of a typical papule revealed the tuberculoid structure seen in the other patients.

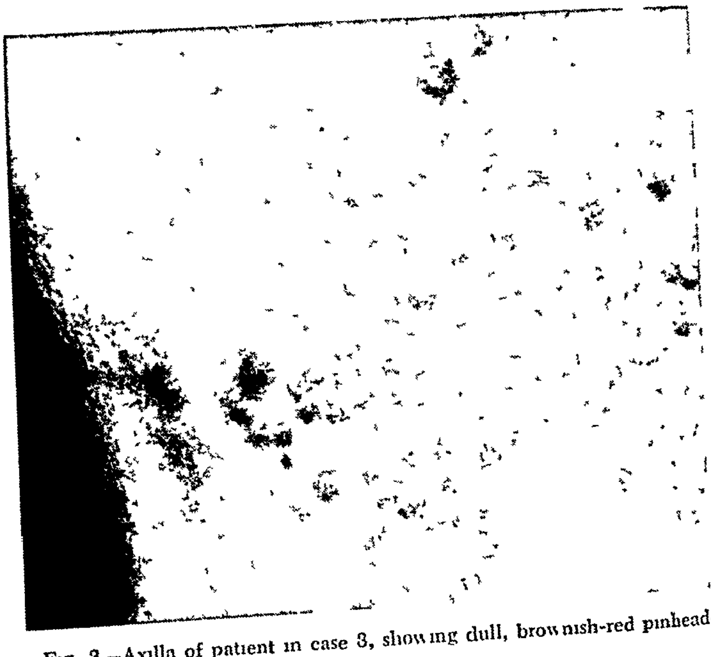

Fig. 3.—Axilla of patient in case 3, showing dull, brownish-red pinhead-to-matchhead-sized papules.

Comment

In each of the four cases the histological sections showed a similarly striking microscopic pattern. The composition of the deodorant stick used by the patient in case 2 is as follows: glycerin, 3% by weight; Carbitol, 3; dichlorophene, 0.375; hexachlorophene, 0.375; alcohol (SDA no. 40), 50; water, 9.45; sodium stearate, 8.5; propylene glycol monostearate, 2; cetyl alcohol, 1; sodium zirconium lactate solution, 22; and perfume, 0.3. The stick deodorants used by the patients in cases 1 and 3 were also "gel"-type sticks containing sodium zirconium lactate. The granuloma in case 4 was caused by a lotion-type deodorant that contains chlorhydroxyaluminum sulfate, but no zirconium.

Fig. 4.—Photomicrograph of section prepared from biopsy specimen of papule of patient in case 3.

An attempt to demonstrate the presence of zirconium in a biopsy specimen from the patient in case 3 was reported by A. E. Osterberg, Ph.D., of Abbott Laboratories, as follows: "This sample, which when desiccated weighed only 0.563 mgm., did not show any zirconium by spectrographic analysis. This means that there is less than 0.3 mcg. of zirconium present. Since the sensitivity of spectrographic analysis is of the order of 0.3 mcg. of zirconium, it is suggested that a biopsy specimen of 10 mgm. would increase the sensitivity and give a more positive determination."

Patients seen by us subsequently, and some reported to us by other dermatologists, have in some instances shown more diffuse erythema and more severe pruritus of irritant reaction in addition to the tuberculoid-type reaction. Other patients have shown evidence of overtreatment dermatitis, and the characteristic papular eruption became evident only after the acute process had subsided. In all cases the condition has been chronic and resistant to therapy, apparently does not respond to x-ray therapy, and is only ameliorated by use of topically administered steroids.

As yet we have no proof of the cause of the unusual reaction observed, but we are investigating the role of sodium zirconium lactate, the entire deodorant preparation, and its individual components. The role of abrasion is also being investigated, because of the appearance of some lesions in lines, suggesting occurrence in razor abrasions. The deodorant preparations used by several of the patients suggest in their advertising that they may be used immediately after shaving the axilla.

Summary and Conclusions

In four cases of a new and unusual type of eruption in the axillas due to deodorant and antiperspirant preparations, the clinical appearance was characteristic and the histopathological pattern revealed a characteristic granuloma suggesting a tuberculoid reaction. Since the original patients were observed, 11 others have been seen by members of our group. It appears that these cases are becoming more frequent. Therefore, further study is indicated to trace the offending mechanism.

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Dr. Frederick J. Szymanski reviewed the histological sections for this study.

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Cancer Concept.—The specious statements that "nothing is known about cancer" and "no man knows the cause of cancer" are commonly made, thoughtlessly no doubt, by medical men who should know better. Thousands of articles in journals and books in medical libraries bear witness against them, as does the unceasing work of the many competent investigators in well-equipped laboratories, who daily produce cancers at will. A great deal is known about hundreds of cancers, and known causes run into hundreds as well. Moreover, doctors daily diagnose, treat and cure indubitable cancers as they do other diseases. . . . The cancer concept depends on a sharp change in behavior observed in body cells themselves. It is a change in which, relative to the rest of the body, they themselves play the part of an invading agent almost as foreign as that of a different form of life such as a bacterium or a virus, and that in a medium not altered otherwise than by the consequences of the change itself. These altered cells no longer conform internally or in external relationships to the regular pattern that characterized their predecessors, but now breed true in a persistent divergence from that pattern. . . . The cancer cell still wears the insignia of a body cell, but its proliferation no longer keeps the old line or subserves the needs of host-tissue maintenance. The new tissue develops a local imitative, inconstant pattern of its own, acts as an intruder and disturbs the general metabolic balance of the body. The change belongs to the cell and persists whether the inducing agent is discernible or not. Disappearance of the agent does not result in restoration of the status quo.—Sir Peter MacCallum, The Place of Surgery in the Treatment of Cancer, *The Medical Journal of Australia*, March 3, 1956.

tant treatment. These persons are to be made as comfortable as possible. They are given adequate doses of morphine, if available, and placed in the lowest priority group for evacuation and definitive treatment. They do not receive therapy until all patients are cared for in the higher priority groups.

The major effort of available medical personnel should be directed toward administering therapy to casualties having from 15% to 40% involvement. If the entire 40% are deep burns, such persons should be placed in the expectant group. Some casualties with 20% superficial burns might be discharged to self-care.

Percentages are not necessarily hard and fast areas of delineation. Each patient should be evaluated according to the depth of his burn, the area of involvement, and his ambulatory state. Since most of the burns are expected to be flash burns, a large number of partial-thickness burns will occur. If the burning insult occurs following secondary fires, however, the depth and extent of injury might be increased.

Casualties having burns involving less than 15% of the body surface should be discharged to self-care if the location of their injury does not interfere with ambulation. Although many individuals having burns that involve 15% of the body surface are hospitalized today, experience has proved that most of these patients can take care of themselves if they can be supplied with water, food, electrolytes, and antibiotics. In a disaster situation, however, self-care will not be feasible if a casualty has a severe burn of the face, if edema interferes with sight, or if a deep burn of the leg makes ambulation impossible. Casualties who have partial-thickness involvement of 15% of the trunk might care for themselves. Many individuals with minor burns might be utilized to help care for the more seriously injured.

In the event of thousands of casualties, it is expected that most of those who survive will be those with burns of such configuration that they can care for themselves. Many casualties who have slight full-thickness involvement might be expected to care for themselves initially and then receive treatment later in a hospital where grafting can be performed. Casualties who have minor second-degree burns might be expected to care for themselves; at the same time they might either assist in the care of other individuals or resume their regular tasks.

It is expected that most of the sorting will be carried out by the casualties themselves. It is hoped that those who can continue to carry on some type of work might make themselves useful and not overburden the medical facilities.

Supportive Therapy

The main type of initial, supportive therapy is supplying water and electrolytes. Normally the patient's loss of sodium and fluids is replaced by intravenous administration of lactated Ringer's solution. In time of disaster, such replacement therapy will have to be carried out by means of orally given electrolytes. A solution of salt and soda made by placing 3 gm. of salt and 1.5 gm. of sodium bicarbonate into 1 liter of water is an effective solution for replacement therapy. Should the number of casualties be relatively small, with an adequate number of trained medical personnel available, then fluid therapy might be given intravenously. It is doubtful whether the subcutaneous route would be of much value, because fluid and electrolytes are not absorbed rapidly in a burned individual.

In order to provide a replacement solution, it might be possible to have salt, soda, and some type of water-purification tablet placed in small packages to be given to burned patients for mixing with water. The salt-soda solution is well tolerated by burned patients. It provides good replacement of electrolytes for the first 48 hours when the burns are not extensive. Any burned casualty who is to be treated, such as those sustaining an injury of less than 40% of the body surface, could probably receive adequate replacement therapy by the oral route. Burns with deep involvement will require later colloid and blood therapy. In most instances, this supportive therapy will not be available within the first few days. There is ample evidence to show that, unless a burn is very deep, burns involving less than 40% of the body surface can be treated initially without whole blood. The anemia that usually follows such an injury should be corrected later.

Although burn therapy for moderate-sized wounds may be undertaken in a hospital without giving antibiotics, it would be desirable to use antibiotics in casualties discharged to self-care. The main reason for such prophylactic therapy is to prevent severe infections caused by beta hemolytic Streptococcus (Lancefield group A). Since this organism is sensitive to most antibiotics, any broad-spectrum antibiotic given orally should be sufficient for the first few days after injury. At the time a casualty receives the salt-soda solution, he might be provided with a sufficient amount of a broad-spectrum antibiotic to last him for several days.

Since tetanus is a potential threat in burned patients, it is advisable to give antitetanus therapy as soon as it can be obtained. Almost without exception, all military personnel are immunized against tetanus; hence, a single injection of tetanus toxoid is all that will be necessary for this group. In the event of large numbers of unimmunized casualties, antitoxin should be administered if available. However, it will be exceedingly difficult to undertake such therapy because of the tremendous amounts of serum needed and the large number of trained personnel necessary to administer this antitoxin.

It will be almost impossible to provide food of high-protein content for a vast number of burned patients. Therefore, it might be possible to provide some type of powder having high-protein content that can be taken with water as a dietary supplement.

Wound Care

Although the present belief is that most burns have less chance of becoming infected when they are cleansed, such a procedure will be impossible in a disaster situation. There is ample evidence that the lack of cleansing is a minor compromise, especially when burns are exposed. In the event of a disaster, almost all burned areas will have to be treated by the exposure method because few dressings, if any, will be available. Should the disaster occur in a cold region, it will be necessary to furnish blankets or some type of covering for the casualties. If time permits and dressings are available, they should be utilized on individuals who would benefit most from their use. It might be wise to prepare some type of mittens for use on burned hands. If flash burns occur on the hands and face, a burned casualty discharged to self-care can be more effective as a soldier or an assistant if he has something to cover his hands and if he can see.

There has been considerable thought and a great deal of discussion concerning the use of a bland ointment for painful second-degree burns. However, most second-degree burns weep; and, as soon as the initial layer of plasma dries, they are no longer painful. In special instances, such as in the case of a combat soldier, it might be wise to give him some type of bland ointment to cover the burned surface. This would offer him some immediate relief. Psychologically, at least, this would make him feel that his burn had been treated, and he would be able to return to duty as an effective combat soldier. The type of ointment to be used in such situations is now under study. When a selection is made, it is believed that the individual soldier can be issued a small tube of ointment that can be inserted into his first-aid packet.

Burn Centers

Some thought has been given to the initial management of burns in time of disaster. Little discussion has resulted on what might happen to vast numbers of casualties after the first few days. In a military disaster, if the tactical situation allows, the burned soldiers may be moved to a particular area designated as a burn center. If this center is located several miles from the disaster zone at a specified fixed installation, all burn casualties will be cared for in this vicinity. On the other hand, if burned casualties have to remain within the area where they are injured, it might be possible to collect them in a certain region or in a large building. Later care should be given in an installation especially designated for burn therapy. Still another phase of sorting or triage, as this procedure is termed by military physicians, might be necessary in the so-called burn center. Casualties who are able to return to duty after one grafting procedure should be taken to the operating room first.

The difficulty in dealing with thousands of burned casualties is to find space in an operating room and time to carry out the multiple grafting procedures that are necessary. Once the casualties who are able to return to duty after one grafting procedure are treated, the remainder can receive grafting operations according to their needs. In many instances, casualties may need coverage of large, open burned surfaces before space in an operating room is available. The loss of protein and electrolytes through large granulating surfaces might be prevented by means of cadaver homografts. These homografts might be laid on the wound when a dressing is changed. This procedure serves as a biological dressing until space is available in the operating room for autografting. It is ideal for those patients who are to be grafted with their own skin to have complete coverage at the time of initial surgical intervention. If there is insufficient time or if conditions are not such that the wounds can be covered completely at the first grafting procedure, then the autografts should be put on and the remainder of the open granulating areas should be covered with homografts. In this manner, each patient will have complete coverage after the initial grafting procedure. This is necessary because a considerable period of time might elapse before space in the operating room is available for a second grafting.

One of the great needs in a burn center is the provision of blood and some type of high-protein therapy. Large quantities of protein are lost after a burn injury, and skin grafting will take well only as long as a patient does not become completely depleted of his protein reserves. A patient may remain in negative nitrogen balance for a prolonged period; but if he does not deplete his reserves then autografts and even homografts will take. It is a real problem to prevent protein depletion. It is doubtful that adequate protein diets can be served if thousands of casualties are involved. Protein-replacement therapy will have to be carried out by a palatable protein supplement that can be given several times a day.

In grafting procedures, it is desirable for large sheets of skin to be placed over flat surfaces. If surgeons skilled in burn therapy are not available in the event of a vast number of casualties, it will be necessary to compromise on the grafting procedure. Any surgeon can take skin from a person if electric dermatomes are available. If the problem involves large granulating surfaces, the autografts should be cut to postage-stamp size, instead of being applied in large sheets, as these grafts can cover a much larger surface. The cosmetic effect, however, is far superior if sheets of skin can be used.

Summary

In the event of a mass casualty situation involving the use of nuclear weapons, it is obvious that major compromises in burn therapy will be necessary. These compromises will be mandatory in all phases of burn therapy, from early resuscitation to late grafting procedures. In the early phase, therapy to be considered includes (1) oral electrolyte therapy, (2) use of the exposure method except when an individual might be rendered effective by the use of dressings, (3) omission of local wound care involving an operating room, (4) orally given antibiotics, (5) self-care or "buddy system" treatment for all burns involving less than 15% of the body surface except in critical areas such as the face and feet, (6) concentration of care for casualties having burns involving 15 to 40% of the body surface, and (7) low priority for evacuation and treatment for all persons with more than 40% of their body surface involved, providing most of the burn is a full-thickness burn. In the later phases, therapy to be considered includes (1) cadaver-homograft skin applied as a ward procedure, (2) autografts applied in postage-stamp size rather than in sheets, (3) protein supplements by oral ingestion, (4) first priority for grafting of patients with small areas of burns because of early discharge from the burn center, and (5) delay in grafting procedures on many casualties beyond the optimal per
In time of disaster, it will be impossible to exc
full-thickness burns or initiate routine rehabil

IMPACT OF NUCLEAR WEAPONS ON MILITARY AND CIVILIAN MEDICAL ORGANIZATIONS

Brig. Gen. Major S. White (MC), U. S. A. F.

• *Successful offensive tactics in nuclear warfare depend on the development of small, mobile, self-sufficient tactical elements capable of rapid dispersion and regroupment. Successful defense similarly depends on the development of units that will not offer an easy target for a nuclear weapon; they must be flexible and mobile, yet linked by centralized control. The medical support, in particular, must include casualty-treatment units widely dispersed in each community and capable of operating for short periods with communications destroyed. All individuals therein must be trained in first aid for assistance to both themselves and others; organic medical support attached to tactical units must be as small as possible; all other supporting medical units must be mobile, widely dispersed, and centrally controlled; rapid transportation must be available. Individuals concerned with medical care must be available for transfer to and from distant areas, and they must be under some type of disciplinary control, the nature of which, whether civilian or military, should be decided before the emergency arises. Experience gained from a joint Army and Air Force maneuver in 1955 demonstrated these points, but the pattern can also be adaped by civilian communities to the problem of supplying medical care under disaster conditions.*

National defense today is based upon preparation for both general and local wars. In either type, nuclear weapons will play a predominant part. These weapons will be highly selective in their action. They may be used tactically in the local or "limited" war to pinpoint relatively small military targets, or they may be used strategically in a general or "all-out" war to destroy large industrial centers. The three defense forces of the United States—the Army, Navy, and Air Force—are redesigning their combat and support units, which include medical organizations, to meet the requirements imposed by this type of warfare.

Combat units have always striven to obtain the maximum of mobility, in order to gain the initiative, to achieve surprise, and to concentrate fire power. Extreme flexibility must also be obtained. To do this, tactical elements must be small, mobile, self-sufficient, and capable of rapid dispersion and regroupment. One of the main objectives of this type of organization is to present as small a target as possible for a nuclear weapon. Medical support for these new combat needs can be readily met by the inherent flexibility of most of the nation's military medical units. However, area and centralized control are the factors that must be added to permit support on a local or regional basis.

"Exercise Sage Brush" Tests

The organization of military medical support for atomic warfare is illustrated by examples from the joint Army-Air Force maneuver "Exercise Sage Brush" held in the fall of 1955. During this period, 140,000 soldiers and airmen from units throughout the United States participated in the largest joint maneuver held since World War II. The primary purposes of the exercise were to train units for modern combat and to test new techniques and weapons. Therefore, simulated atomic weapons and numerous means for their delivery were made available to the commanders of both the defending United States forces and the invading aggressor forces.

In a nuclear war, as this exercise was, it is axiomatic that for both survival and victory the first order of the day is to obtain air supremacy. This is gained by destruction of the opponent's air power through an air war. Once air supremacy is achieved, freedom of movement is assured for one's own ground and air forces, with denial of this freedom to one's opponent. Air forces can then support ground troops in the exploitation phase of war or in the elimination of any enemy ground troops that might remain. In Exercise Sage Brush, the hope for initial survival of all forces was based on the wide dispersion of tactical units. As can be seen in figure 1. dispersion caused the distances over which the maneuvers took place to be extensive. Air bases of the opposing air forces involved in the air war are shown spread throughout 13 states of the southeastern United States. The shaded portion of the map indicates the ground area in Louisiana over which the field armies maneuvered.

Air Force and Army Organization

In the air forces, the dispersion shown ensured that a wing of 75 aircraft would not be based entirely on one airfield. To have done so would have made possible the destruction of the wing's three squadrons through the successful delivery of one atomic bomb. Therefore, all of the wings were divided, with one squadron or less assigned to any single air base. The problem of supply to these dispersed units was met by the use of air transport. This air transport was. in turn, available for the evacuation of medical casualties and governed the organization of air force medical support that was provided in two ways: one, through the organic medical personnel and equipment assigned to a squadron; the other, through an area support unit covering the entire theater. The squadron medical unit consisted of

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Read before the Section on Military Medicine at the 105th Annual Meeting of the American Medical Association, Chicago, June 14, 1956.

a flight surgeon and three enlisted aeromedical technicians. This team was equipped with a compact air-transportable dispensary. It provided for early treatment and for the aviation and preventive medicine care that was considered the minimum essential in the squadron and relied on evacuation to theater units for further medical support. Theater area support was organized into a tactical aeromedical wing under the centralized control of the Air Force commander. This wing consisted of units varying from small 36-bed air-transportable infirmaries to 150-bed fly-away hospitals. It also included an aeromedical evacuation group and other elements for dental, veterinary, laboratory, and preventive medicine services as well as for medical supply. All hospitals had their personnel organized into several disaster teams, consisting of physicians, nurses, and auxiliary helpers. These teams, with emergency supplies, could be detached and sent to the assistance of areas incurring large numbers of casualties.

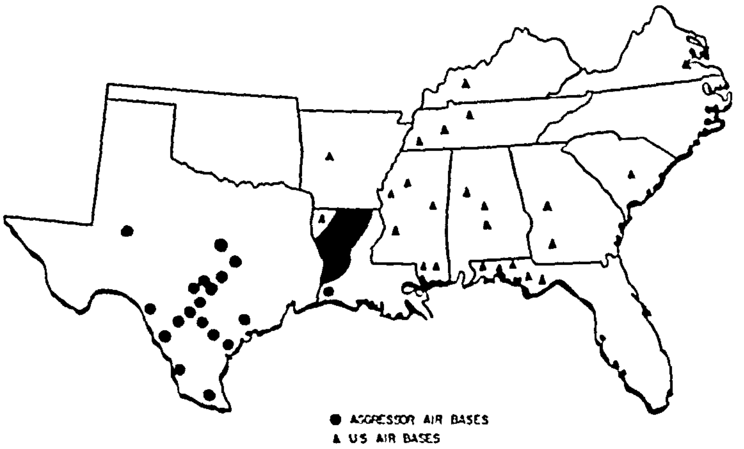

Fig. 1.—Extent of maneuver area in Exercise Sage Brush, showing Air Force units in 13 southeastern states and Army troops in shaded area in Louisiana.

Through centralized control, flexibility of assignment was possible. Hospitals and other units were based in areas where the greatest work load was expected or were moved rapidly in whole or in part as the tactical situation dictated. Need for such control will be even more acute as greater dispersion becomes possible in the future, with combat aircraft developing vertical take-off and landing capabilities. Then squadrons will be dispersed in elements of one or several planes. The contined adaptability of medical support for such a situation was demonstrated in Exercise Sage Brush, when squadrons were dispersed in small elements through the assignment of an aeromedical technician with each element and flying visits by the squadron flight surgeon.

Army forces, similar to the air forces, also had their units organized into the smallest possible tactical elements for self-sufficiency and dispersal. In the forward battle zone, or division area, the medical elements organic to the division were used for early emergency care. Direct support of these units and area medical support in the rear were provided by 300-bed to 400-bed field hospitals. These functioned as one complete unit or were partitioned into independent elements of 100 beds each. In addition, evacuation hospitals, medical supply depots, and clearing and ambulance companies provided support under the control of a centrally located medical group headquarters. Aircraft also were used, as in the Air Force, to supply isolated units and evacuate transportable casualties. For both ground and Air Force troops, supplemental medical supply units were available for delivery to organizations suffering large numbers of casualties. The supplemental supplies were designed around a basic unit of drugs and dressings needed to care for 100 casualties of the type expected in nuclear warfare. Multiples of this basic unit were delivered as required, depending on the number of wounded reported.

The experiences of Exercise Sage Brush demonstrated that, with a rapidly changing tactical situation and the occurrence of mass casualties, it was necessary to have a headquarters exercising centralized control. In the event of destruction of the central headquarters, control was passed to an alternate headquarters. Under such guidance, medical organizations were used to their full effectiveness, as it was possible to assign them throughout the combat area as needed. Good communications and airlift were also essential for successful operations. In their absence, as occasionally did occur, it was necessary for an isolated unit to rely on its self-sufficiency. Self-sufficiency means, among other things, that each individual of a unit must be well trained in the principles of first aid, for administration to himself and to others. Such training will in many cases provide the only medical care available initially after an atomic bomb strike.

Destruction from Nuclear Weapons

The extent of damage and the pattern of a nuclear war is seen in figure 2, which illustrates the bases of the United States air forces that were destroyed by aggressor atomic air attacks in the first two hours of the maneuver. The magnitude of any single bomb burst shown can be appreciated if a comparison is made to the high-explosive bombs dropped by air during World War II. If every bomber plane of the allied air forces of the United States and the United Kingdom had been loaded to capacity with high explosives and all had dropped their bombs in one satu-

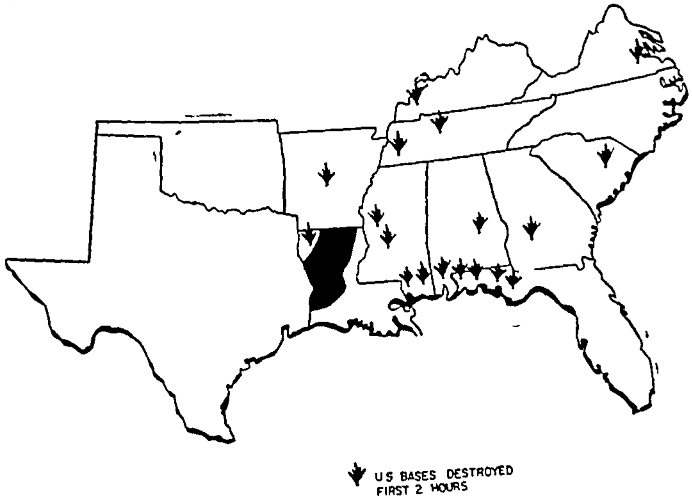

Fig. 2.—U. S. Air Force bases destroyed by atomic bombs in first two hours of Exercise Sage Brush.

ration raid, the result would have been only a fraction of that represented by a single atomic burst in figure 2. Similarly, figure 3 shows the number of atomic weapons used on ground troops during the entire maneuver. Again, the devastation shown is catastrophic. As a result of such action, it is evident that past experiences of destruction covering time periods of months and years are now compressed into periods of minutes and hours. The decisive phase of a war may be over in a few hours or days, as it was in this maneuver. On the other hand, it is possible that a war might be prolonged due to many factors, political or military. In the latter instance, the type of medical support provided in Exercise Sage Brush would have been adaptable to the situation, because of the flexibility of medical units and the availability of airlift. Air transport could have moved medical support as needed and cleared casualties from forward areas to well-equipped hospitals in the rear. Thus, tactical units would have been relieved of a logistical burden and would have preserved their ability for rapid movement and exploitation.

Principles for Organization of Medical Groups

Lessons learned from this maneuver indicate that our Army and Air Force medical organizations in existence and being developed can cope with the problems of nuclear and thermonuclear warfare if certain principles are followed. These principles are as follows: 1. All individuals must be trained in first aid for assistance to both self and others. 2. Organic medical support attached to tactical units must be of the smallest size possible. 3. All other supporting medical units must be mobile, widely dispersed, and centrally controlled. 4. Rapid transportation must be available.

These same principles can apply to the organization of civilian medical groups in preparation for any disaster. If adapted to civil defense, it would mean that first-aid and self-aid training must be given to all citizens. Casualty-treatment units must be organized in advance to be manned by designated physicians and helpers. These units must be widely dispersed in a community and be capable of operating for short periods with communications destroyed. Large hospital units must be organized on a team basis for dispersal or for sending assistance to other areas. Similarly, all means of transportation for both supplies and patients must be organized on a team basis for local or regional use. Plans for centralized control of all elements of medical coverage must be developed in each geographical area. Each community must coordinate with neighboring areas on disaster plans. Local and state governments must be prepared to furnish regional aid. It is conceivable that, as plans progress, a national, central control headquarters will be required to coordinate the individual efforts of military and civil agencies.

Relative to civil defense, it is appropriate to quote I. S. Ravdin,[1] who has outlined the action he felt necessary as follows:

> Civil defense on a local or even a regional basis is, in my opinion, unrealistic. We must develop a plan that will permit the transfer of those concerned with medical care from distant areas and the assignment of those available at the local area. Whether these individuals will be under complete civilian control or whether they will, once they are called to duty, be under military control should be decided before the emergency arises. What needs to be recognized now is that they must be under some type of disciplinary control. The future can not be left to chance.

Summary

Thermonuclear warfare requires that military tactical units be small, dispersible, and self-sufficient and that they possess extreme mobility and flexibility. Medical support must be adapted to this type of organization. This is done by providing in a tactical unit only the medical personnel and equipment to give minimum essential early treatment and preventive medicine supervision. Additional support is given by use of mobile medical units assigned on a regional basis as required, through centralized control. Air transport is used to supply dispersed units and to evacuate patients. Examples of the use of this new type of organization were illustrated for both Army and Air Force units in the large joint maneuver "Exercise Sage Brush" held in the fall of 1955. Civilian communities can organize along similar lines to furnish medical care under disaster conditions. This concept provides for dispersed medical units, use of self-aid, and support through mobile units under centralized control.

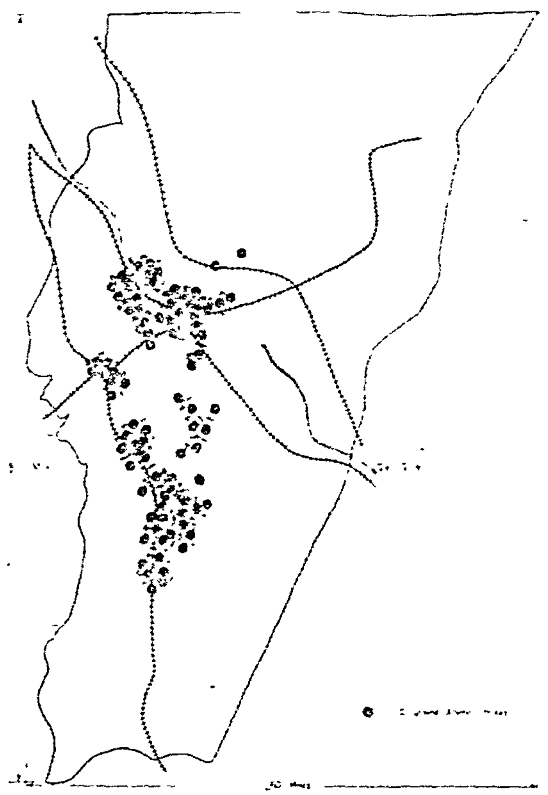

Fig. 3.—Total of atomic weapons used on ground troops during Exercise Sage Brush.

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ROLE OF THE GENERAL PHYSICIAN IN THE ATOMIC AGE

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• *It is essential for all physicians, and particularly the general physician, to be alerted to the new health and hazard problems related to the peacetime use of nuclear radiation. This knowledge will also aid him well in event of atomic warfare.*

The use of radioactive substances alone has increased tremendously in industry, pharmaceuticals, and medicine in general. Employment exposures to nuclear products impose an immediate responsibility to the physician to be aware not only of the side-effects of radiation but more so of the diagnosis and treatment of overexposed patients. The complaints of malaise, lassitude, and anorexia unsupported by the usual clinical causes; gastrointestinal symptoms; dermatological conditions; or bizarre or unrecognized hematological changes in those patients working with or in the vicinity of nuclear radiation should alert the physician to consider these symptoms as perhaps manifestations of overexposure to radiation.

Today the supposed safe limit of 300 mr per week total body exposure is only approximate and not conclusively free of danger. Even those patients not overly exposed may develop "radiophobe" attitudes, with obsessions necessitating careful and patient guidance by the physician.

This is a new branch of clinical medicine, still not propounded in the medical literature nor included in the medical school curriculum, yet it faces some of us today and will face many of us in practice in the near future.

I am extremely grateful to the members of the Section on General Practice for having honored me with the chairmanship in the past year. A number of subjects suitable for presentation as the chairman's address were considered, some were reconsidered, some were written about and the articles published in various medical journals, and others were discarded. In my review of the medical progress of the past decade and the effects of such progress on the general physician, I found that the swift tempo of research has been so overwhelming that it is often difficult for any physician, whether specialist or general physician, to remain abreast. This is particularly true if one tries to grasp the impact on medicine of the development in nuclear physics.

Research in Nuclear Radiation

The amount of research already done in the field of nuclear radiation must be tremendous. To realize this, we have merely to use our powers of logical inference, based on the spectacular results we have been permitted to view. The greatest portion of this research is not published, for reasons of national security.

At a meeting held in Washington, D. C., on April 28, 1955, on "Nuclear Radiation Hazards and Their Political Implications," sponsored by the Federation of American Scientists, Dr. M. Stanley Livingston, professor of physics at the Massachusetts Institute of Technology, remarked in his opening address upon the extreme difficulty of securing enough qualified persons to fill the panel. Many scientists hesitated or were not given clearance to speak on a subject about which so much information was still being classified. Others declined to enter the discussion for fear of involvement in an issue sufficiently controversial to provoke security clearance trouble. Thus we see that much of the work done in nuclear radiation has not been made available to the medical profession in general and cannot have been exposed to the acid test of widespread clinical observation.

Present Dangers in Atomic Medicine

Dr. Bentley Glass, geneticist and professor of biology at the Johns Hopkins University, states that there are two grave dangers in the present situation. One is our ignorance about the effects of radiation, and ignorance is always a danger. The other concerns the matter of "average" dosage. As the number of test explosions increases and the long-lived isotopes accumulate and as the industrial atomic energy plants multiply and the disposal of atomic waste products becomes more and more a critical problem, the cumulative exposure to radiation may exceed the "safe dosage" of 0.2 r per year, which was the average amount received by the Oak Ridge and Hanford workers in 1949.[1] This leaves me with the frightening thought that, when the bulk of atomic research is finally dumped into our laps and literature, we physicians will have to assimilate the mass of it, rather than the slow piecemeal of it as we would prefer.

I firmly believe that the discovery of nuclear radiation will produce the greatest change in the lives of mankind since the discovery of fire. I believe that the amount of productive atomic and radiation research and the use to which this research will extend in medicine in the very near future will far surpass that of any group of new drugs discovered in the past 50 years—and this includes the steroids and antibiotics. I also believe that our historians will refer to the 20th century as the atomic rather than the antibiotic age of medicine.

No doubt, the atomic age will be said to have begun at that point in time when man learned not only how to release, but also how to control, the energy that binds the nuclei of atoms. The "control" part appears to be the knottier of the two problems at present. In fact, the peacetime atom may thrust on the general physician a whole new set of health and hazard problems, many of considerable magnitude. We can be certain that in the near future we will be living in a world more radioactive than at present, since the use of atomic or nuclear radiation will steadily increase in industry, hospitals, pharmaceutical manufacturing plants, metallurgical research, biological research,

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Chairman's address, read before the Section on General Practice at the 105th Annual Meeting of the American Medical Association, Chicago, June 12, 1956.

atomic submarines, aircraft carriers, plastic industries, and many other aspects of our technical culture. In all of these, we physicians may find the invisible hazards more insidious in onset and more frightening in climax than any of the dramatically visible occupational hazards we occasionally encounter at present. Even with the best equipment and protective devices, there is always present the potential danger of radiation leakage, unforeseen accidents, and that common frailty—human carelessness. Furthermore, we have with us always the accident prone, and no safety equipment has yet been devised that will shield them from themselves.

Perhaps I had better pause right now to assure you that this paper has nothing to do with atomic warfare. It is not my purpose to discuss the role of the military in the use of nuclear power but rather the role of the general physician, the "front line physician," in this, the atomic age, which is rushing down the corridors of time to meet us head on. And we, I might add, are unprepared for the encounter. Most of us are babes in the wood where the problems and potential results of exposure to nuclear radiation are concerned. If I can succeed in alerting even a few general physicians to the fact that a new era is at hand and that we are not prepared, I shall have accomplished the purpose of this address.

Effects of Exposure

In any discussion on the effects of radiation, we must always keep in mind that radiation is absorbed, and that its absorption takes place in the basic biological unit of life, the body cell. The pharmacological reaction to radiation that takes place in the body cell is much like that of drugs. Both produce local as well as general (systemic) effects. These effects may appear immediately or after varying amounts of time, both may produce morphological as well as functional changes, and drugs as well as radiation produce reversible as well as irreversible effects. Here the similarity between drugs and radiation ends. The reversible effects of cellular drugs (such as anesthesia) is a common fact in the field of pharmacology and is familiar to all physicians. But the reversible effects of radiation, though theoretically possible, have been demonstrated only through artificial interference by such means as cooling or washing the irradiated tissues. Unless such interference is introduced, irradiated cells and tissues are damaged irreversibly.[2]

In many instances, the apparent increase in function of irradiated cells is an expression of premature aging.[3] After exposure to radiation doses that do not produce cell death immediately, vital functions proceed at an accelerated pace until cell death occurs. Vital energies are exhausted prematurely due to the impact of irradiation and the disorganization of factors controlling the orderly use of these energies. We are well acquainted with the example of how menstruation may be stimulated when irradiation of the ovaries is attempted. Here the therapeutic result is achieved at the price of partial destruction of the atretic graafian follicles, which causes the amenorrhea, and at the possible further price of inducing hereditary changes in the ovary of the irradiated woman.

The knowledge of the side-effects of irradiation is an unqualified necessity and is indispensable in the clinical diagnosis and treatment of patients exposed to radiation. The effects of radiant energy on living matter, particularly of humans, is of the greatest importance to all physicians, especially the general physician. We must be capable of evaluating these effects as either therapeutic or toxic. The ever-increasing use of radioactive substances in recent years is borne out by these figures. It has been shown that the use of radioactive iodine has increased from a few millicuries to almost 50,000 mc. per month; and that radioactive phosphorus has increased to almost 13,000 mc. per month; and radioactive gold, which was almost unknown in 1950, is now being distributed at the rate of more than 50,000 mc. each month.[4] This vast increase in the use of these radioactive drugs in so short a time certainly shows that there is a definite radioactive pharmaceutical business in progress.

The utilization of ionizing radiation for the purpose of sterilization of drugs and foods, suture materials, and other pharmaceutical agents opens new fields for the peacetime use of atomic energy. I would like to mention some of the sequelae of the atomic age of concern to physicians in general practice.

In a recent issue of THE JOURNAL, a case of aplastic anemia secondary to intravenous therapy with radioactive gold was reported.[5] On Jan. 11 and 12, 1956, newspapers carried the story of four men who, having been exposed to radioactive cobalt, faced weeks of uncertainty as to the results of this exposure. It seems that one of these men needed a piece of string and picked up the first piece he came upon at his place of work. This piece of string, unfortunately, had a capsule of radioactive cobalt attached to one end. This radioactive cobalt capsule was used in the steel plant to detect defects in structural steel and piping. How long he held it in his hand is unknown, but it eventually reached his pocket, and when he arrived at his car he transferred the string and cobalt to the glove compartment. The other three men were riders in the car and thus were innocently exposed to radiation. Here is but one example of the carelessness and ignorance I mentioned, and this may very well be repeated many times over in the next decade. This example is cited in order to show that we general physicians must be prepared at all times in the future to see patients in our offices who are walking demonstrations of careless and ignorant exposure to these atomic forces.

Examination of Patient

Let us now explore the potential physical findings we general physicians might uncover in this type of patient were he to visit us in our offices, not knowing he had been exposed. In this paper I cannot cover completely all of the findings, diagnoses, and treatment of radiation exposure. Physicians and scientists much more learned in this field than I am have contributed a great deal to present-day medical and scientific literature. It is my purpose to [illegible] few of you to learn all you can about this [illegible]ching atomic era in medicine so that [illegible]ared for the oftentimes [illegible] sympt[illegible]

Just as important as the meticulous history will be the place of employment, the type of material with which the patient might be in contact, and whether the patient is in his routine work exposed to ionizing radiation in any of its forms. Some of the most important early complaints our patients might present could be malaise, anorexia, and lassitude. When these complaints are not supported by other usual clinical causes, they may very well be the first expressions of an overexposure to radiation. These signs are of the utmost importance: Exposure in any of these patients may be due to careless handling of material, an undetected breakdown of protective measures, or simply the expression of unusual constitutional sensitivity of the patients to ionizing radiation. This could occur in such persons as those with vagotonic conditions—in spite of observation of and strict adherence to all safety measures. Later there may be a low-grade nausea, possibly with vomiting or diarrhea or both, which might very well be attributed erroneously to other diseases or infections. But if we are vigilant and never fail to consider the irradiation exposure potential of patients employed where such exposure is possible, much time will be saved in arriving at the probable diagnosis.

A careful examination of the skin, hair, and fingernails is mandatory in any patient working in plants using radiation. The presenting complaint may be simply itching of the skin, a burning sensation, or perhaps nothing but a slight reddening of the irradiated exposed areas. The physician might be confronted by an unexplained pigmentation, one not conforming to the usual problems in dermatology in general practice. Here again the accurate history is most important. Symptoms such as abnormal epilation of the scalp in women or of the face in men should alert the physician to the possibility of radiation exposure.

Exposure may produce a burning sensation of the eyes with undue lacrimation.[6] Any cataract formation, especially on the posterior pole of the lens in young persons, should arouse suspicion of exposure to radiation. The reaction in the blood stream will be of the utmost interest to the general physician. The systemic effects of prolonged exposure to irradiation are serious. There may be aplastic anemia with fatal termination.[7] And chronic exposure may increase the incidence of leukemia.

It has been shown in the writings of Henshaw and Hawkins [8] that the incidence of leukemia in radiologists is approximately 8 to 10 times greater than in other physicians. Must we not consider those working in nuclear industry, unless closely observed and more closely protected, in the same category? The exact dosages required to produce blood alteration with a depression of the peripheral blood elements are not known, but the degree of depression of these blood elements is believed to be the best index of the severity of acute radiation injury and perhaps an index to the amount of exposure.

Complete preemployment blood studies on all of our patients working with, in, or about radiation plants will be of critical importance. These should consist of hematocrit determinations and leukocyte, neutrophil, lymphocyte, and platelet counts. They should, in fact must, be done by physicians experienced in such blood studies; otherwise, the patient's specimens should be sent to a pathologist. Any blood smears from patients exposed to radiation that show a blood picture unrecognizable or bizarre to the general physician should most certainly be dispatched to a qualified pathologist, preferably one schooled in the effects of radiation exposure on the blood. Following this, bone marrow, liver, and spleen biopsy studies may be in order. In the preemployment physical examination of patients applying for positions in atomic nuclear reactor plants or in industries using radiation, it might be wiser to exclude from such employment any person whose total white blood cell count is above or below the recognized upper and lower limits of normal until definite rules and regulations are established by proper authorities for this condition.

Effects of Radiation on Sterility and Genes

The always puzzling problem of sterility will be an added burden of diagnosis and treatment to the general physician and medical men in general, especially sterility in the male patient. It is, and has been, known for many years that the reproductive organs are highly sensitive to radiation. The genes, too, are susceptible, with the production of radiation-induced mutations. The effects in the first generation may not be detectable, but how are we to decide just what will be inflicted on future generations—even if the ancestral dose was small? Literature [9] tells us that the progeny of radiologists and others exposed to radiation are subject to a significantly higher percentage of congenital malformations than those of persons not so exposed. To the general physician, the implications of this finding will be magnified alarmingly when he first encounters malformations and realizes that they will appear even more frequently in subsequent generations. It is not inconceivable that the actual morphology of our descendants may depend upon the vigilance and acuity of physicians practicing today. We must be equipped and ready to detect even the slightest symptom of overexposure, for nowhere in the literature could I find evidence that a method of countering radiation's irreversible effects was even in the offing. There may come a time, however, in our rapidly expanding and forward-moving industrial atomic age when certain short cuts in protection from radiation may occur. This is the danger period.

Maximum Dosages

There is such a thing as the maximum permissible dose of radiation, and this is defined by the International Commission on Radiological Protection as "that dose of ionizing radiation that, in the light of present knowledge, is not expected to cause appreciable bodily injury to a person at any time during his lifetime."[10] It is further stated that the "maximum total dose to which the body may be exposed continuously or intermittently is currently established as 300 mr per week, whereas exposure to the hands and forearms may be five times this amount and still be considered to be within safe limits." But—and here is the most important statement: "These supposed safe limits are only and at best approximations, and there is no conclusive evidence that even such levels are completely free of danger. This maximum permissible exposure rate has been modified and reduced in the past. In the near future with the expanded use of ionizing radiation this permissible exposure rate may have to be modified and reduced further."

Safety Measures

For the purpose of the general physician in his daily practice with those working in or about radiation, irrespective of the safeguards, the wisest precaution to protect patients would be the advice of Ritvo, D'Angia, and Rhodes,[7] "that excess radiation comprises any radiation which can be avoided." It is likewise important that all plants dealing with radiation—in no matter what form—adopt safety patterns calculated to minimize or eliminate all dosages, no matter how small, how infrequent, or how harmless these dosages appear to be.

Many devices have been employed to measure exposure. This represents no problem. The difficulty lies in measuring the individual—and the machine has not been invented that can do this. The pocket dosimeter and the Victoreen ionization chamber can both register the amount of radiation John Doe has absorbed, but John Doe himself remains as unpredictable as he has always been, physicians and psychologists notwithstanding. What his particular physiological reactions will be to even the so-called minimum dose always remains uncertain. What is harmless to mankind may be lethal to one man—and that one man may be your patient, or mine. Thus, to rely upon any instrument to report the amount of exposure and to accept this without further investigation of the individual himself would be to abandon the caution upon which our profession is based and to do a grave injustice to the patient.

Other Problems

Another problem we will undoubtely face will be the radiophobes—patients obsessed with a probably groundless fear of overexposure. This can be complicated by the known effects of radiation on the reproductive organs, since the relationship between sex and the psyche is a familiar one to all of us. Distinguishing a person with bona fide radiation poison from the radiophobe will require skillful diagnostic techniques, patience, and understanding. It is for this reason that the general physician must familiarize himself with the fundamentals of medical radiation biology in order to give competent and confidence-inspiring advice to these patients.

In the past few months in newspapers throughout the country much has been written about proposed nuclear power plants to be erected in the immediate future in this country. True, while we are happy about the enrichment of our national economy through the uses of atomic energy, we, as physicians, must be cognizant of the potential dangers inherent to this industrial evolution. Two very important characteristics differentiate the potential hazards of nuclear fission products from the more conventional industrial poisons. First, fission products in nuclear reactor plants do not assault the senses, even in lethal doses and concentrations. Second, nonlethal doses or exposures can produce permanent injuries that may not become evident for many years after the original exposure. Furthermore, the nuclear fuels, such as plutonium and uranium –233, are highly toxic if inhaled or ingested.[11] It is important for all physicians to know and understand the toxicology of these reactor fuels and of the other products used.

Medical Education and Radiation

To prepare the future physician for the atomic era of medicine, education in the field of radiation biology is a "must" for the medical student, the intern, and the resident. Yet, I wonder how many, if any, medical schools in this country are properly staffed with a separate department to teach radiation biology and the pharmacodynamics of nuclear activity as applied to medicine. Must we wait until the full impact of the entire mass of research envelopes us completely and the literature becomes too complex for orderly sorting before our schools inaugurate adequate teaching facilities and staff in this all-important new field? The longer we wait, the more difficult the task of weighing, analyzing, and sifting the information so that it can be effectively imparted to students.

At the moment we seem to be ensnared in an incongruous situation wherein the physical scientist controls the "atomic pile of education and knowledge," and the physician passively stands aside. Would it not be eminently appropriate to have physicians engaged in full-time medical research in radiation biology teach those who must combat the human side-effects of that research? Physicians may then instruct medical students, interns, residents, and nurses. Needless to say, the obvious benefits would apply indiscriminately to all—to the laboratory scientists and physicians as well as to the general public.

Recently a nine-man study group presented their findings, suggestions, and conclusions to the Joint Atomic Energy Committee[12] on the peaceful uses of atomic energy. This panel maintained that "the speedy progress in atomic medicine depends on three principal factors: training of an adequate number of doctors, nurses, and technicians; construction and staffing of adequate research facilities; and provision for rapid communication of the most advanced medical knowledge." This group further stated, and I quote, "It is our strong feeling, however, that medical institutions and research centers should not assume a passive role and expect the government and more specially the (Atomic Energy) Commission, to assume all or even a major portion of the responsibility for providing research facilities, equipment, and materials." To further substantiate my feelings in the matter of nuclear energy radiation—its use and misuse—this same nine-man group presented a definite six-point program to the Atomic Energy Commission in their report. They stated:

"1. Provide all medical schools with adequate facilities for training in atomic medicine techniques. 2. Create additional research centers with appropriate equipment, including reactors. 3. Design low-cost atomic medical equipment suitable to the needs of the 6,100 hospitals and medical clinics without atomic facilities and provide at least minimal facilities to this group as rapidly as possible. 4. Make available at reasonable prices the

, by management of the patient and his family, a variety of rehabilitative measures—in other by a totality of psychiatric therapy in which the al treatment merely represents an essential ating measure, especially if the physician has eded in avoiding certain undesirable side-effects night potentially aggravate specific psychological s.[1] Shock therapy itself, therefore, does not relieve primary traumatic neurosis that originally evoked the warning or tension anxiety (fig. 1), but it does interrupt the vicious cycle between the warning anxiety on the one hand and panic and depression on the other (fig. 2), thus relieving the secondary traumatic state of the ego,[3] i. e., the secondary traumatic neurosis induced by the warning anxiety itself.

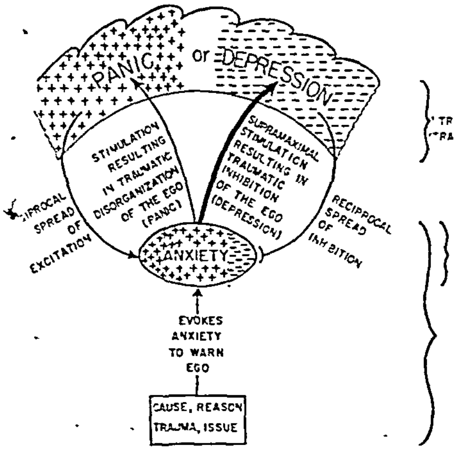
PANIC
or
DEPRESSION
STIMULATION RESULTING IN TRAUMATIC DISORGANIZATION OF THE EGO (PANIC)
SUPRAMAXIMAL STIMULATION RESULTING IN TRAUMATIC INHIBITION OF THE EGO (DEPRESSION)
IPROCAL SPREAD OF EXCITATION
RECIPROCAL SPREAD OF INHIBITION
ANXIETY
EVOKES ANXIETY TO WARN EGO
CAUSE, REASON TRAUMA, ISSUE
SECONDARY TRAUMATIC NEUROSIS TRAUMATIC STATE OF THE EGO
WARNING OR TENSION ANXIETY
PRIMARY TRAUMATIC NEUROSIS

Fig. 1.—Relationship of trauma, anxiety, panic, and depression. + denotes excitation, — denotes inhibition.

How does shock therapy accomplish this result? The paralysis of the ego in the form of depression, resulting as it does from the impact of excessive quantities of excitation by warning anxiety (fig. 1), has all the earmarks of a paradoxical reaction in the Pavlovian sense, in that it appears to be a state of profound inhibition or paralysis induced by excessive excitation. Furthermore, we are justified in assuming that warning anxiety, which is largely unconscious and which can be precipitated or aggravated by an injection of epinephrine, is essentially a subcortical phenomenon. Panic and depression, on the other hand, pervade the conscious mind and cannot be precipitated or intensified by intravenously injected epinephrine and hence appear to be mediated and perceived chiefly within the cortex of the brain.

Electroshock diminishes cortical excitability, and it appears to be for this reason that the subcortical warning anxiety can then no longer overstimulate the cortical ego into panic or depression. The ego and its defenses appear strengthened after electroshock therapy, for the excitation threshold of the cortex has been raised (fig. 2). This dynamic alteration in the threshold gives the ego an opportunity to strengthen and regroup its defenses,[4] a process that can be aided by psychotherapy, although it often takes place spontaneously after successful electroshock therapy.

Warning or tension anxiety, while no longer disruptive to the ego because of the latter's raised threshold to stimulation, can of course still be perceived at certain stages or intensities of treatment. This anxiety may come even more prominently to the fore (fig. 2) because its presence is no longer obscured through its secondary paralyzing effect upon the ego, which in turn had an inhibitory effect upon the anxiety due to spread of inhibition (fig. 1). This obviously explains the apparently reciprocal relationship between warning anxiety and depression that I pointed out earlier, based on the fact that I was able to convert and reconvert one into the other by specific physical measures.[2]

The residuum of warning anxiety, conscious or unconscious, that the patient is likely to be left with after electroshock therapy has to be dealt with in one way or another. Often in his improved state the patient is able to look at the underlying issues that aroused the warning anxiety in a new light, much as we all are able to do with minor problems after a good night's sleep or when we find that something we had dreaded did not materialize. This resurvey in turn diminishes the anxiety engendered by the issue. A beneficent cycle has been set up. A similar result can be brought about by follow-up psychotherapy in patients who may not be able to attain this strengthening and maturing by themselves.

In particularly severe illnesses, massive shock therapy may be utilized to the point where not only excessive response to, but even awareness of, warning anxiety is suppressed temporarily. The disadvantage of this last method is that the warning anxiety is merely suppressed and during the convalescent phase is likely to erupt again disturbingly and precipitate relapse. I prefer release and ventilation of the warning anxiety by the added use of nonconvulsive-stimulation treatment, which enables the therapist to deal simultaneously with it and the underlying issues, thus paving the way for subsequent psychotherapy of the primary traumatic conflict.

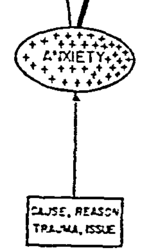
ELECTROSHOCK DIMINISHES EXCITABILITY OF CORTICAL SUBSTRATES OF EGO
EGO BOUNDARIES STRENGTHENED
EXCITABILITY OF EGO DIMINISHED, HENCE EXCITATORY DISORGANIZATION (PANIC) AND INHIBITORY DISORGANIZATION (DEPRESSION) ARE EXTINGUISHED
ANXIETY
CAUSE, REASON TRAUMA, ISSUE

Fig. 2.—Effect of convulsive electroshock therapy. + denotes excitation; O denotes extinction.

Tranquilizing Drugs

The action of the new tranquilizing drugs, chlorpromazine and reserpine, is fundamentally different from that of shock therapy, in that these drugs appear to suppress the primary, epinephrine-precipitable, subcortical warning or tension anxiety while exerting only an indirect influence on the secondary cortical manifestations—the traumatic state of the ego—in inverse proportion to the degree to which important ego functions have been disrupted in the direction of paralysis or inhibition by the anxiety. For this reason tranquilizing medication, especially with chlorpromazine, is most effective in manic states. This may be due to the fact that the manic state is a condition most directly power-driven in the direction of excitation by epinephrine-precipitable tension anxiety, as I pointed out elsewhere,[5] and in which important ego functions are least weakened. Conversely, for the same reason, and in remarkable accord with the fact that inhibitory cortical processes are more readily extinguishable than excitatory ones,[6] manic psychoses are least readily relieved by electroshock therapy, which is an extinction type of treatment, unless the treatment is carried to the point of obliterating even the mere perception of warning or tension anxiety. Another reason for the superb clinical results of chlorpromazine therapy in manic patients is that manic psychoses tend to be of naturally short duration. Hence, if the manifestations of the psychosis can be suppressed for the natural duration of the manic episode, the patient can continue to live a rather normal life and may even be able to keep on working without experiencing either the social disadvantages of morbidity or the undesirable suppression of cortical functioning produced by electroshock.

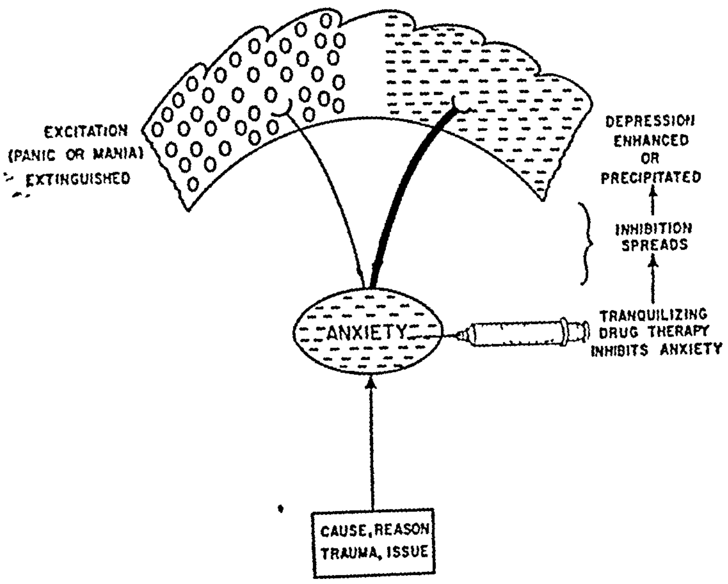

Fig. 3.—Effect of tranquilizing drug therapy. — denotes inhibition; O denotes extinction.

Depression is at the other end of the scale of effectiveness of the new tranquilizing drugs. Chlorpromazine and reserpine not only are entirely ineffective in most cases of depression but are actually contraindicated because they may aggravate the condition. The reason for their ineffectiveness is obviously the fact that, in depression, paralysis of the ego is most profound, the ego being in an inhibitory state already. Inhibition of ego functions is not only not relieved but is actually aggravated by these drugs, because not only has this inhibition of ego functions become independent of continued overstimulation of the ego by the warning anxiety that originally paralyzed the ego into depression but, by a process of negative induction leading to spread of inhibition, the inhibited state of the ego has extended to include the original warning anxiety as well (fig. 1). This fact explains the reciprocal relationship of anxiety and depression in contradistinction to the simple vicious-cycle type of relationship that exists between warning anxiety and panic (fig. 1). Thus it comes about that further suppression of the original warning anxiety by means of drugs will actually deepen the existing depression (fig. 3), or it may even precipitate depression. Conversely, enhancing the warning anxiety by injection of epinephrine, for instance, may relieve depression temporarily.

Depression is indeed the most significant mental and emotional complication arising from the use of these tranquilizing drugs. If administration of chlorpromazine, for instance, is continued too long after control of a manic psychosis (as occurred with three patients in my own experience, in whom this drug was administered over periods ranging from four to seven months in an attempt to tone down mild residual hypomanic states) or if reserpine is given to depression-prone individuals for relief of hypertension,[7] these drugs may precipitate depression, which, however, can be promptly terminated by withdrawal of the drug. Gastrointestinal symptoms of withdrawal of chlorpromazine can be avoided by administration of Donnatal (a combination of hyoscyamine sulfate, atropine sulfate, hyoscine hydrobromide, and phenobarbital), which is then rapidly withdrawn.

The new tranquilizing drugs are less consistently effective in catatonic and excited schizoaffective states than they are in manic states. In catatonic and hallucinatory paranoid states I have found reserpine relatively more effective than chlorpromazine. In most other anxiety and panic states and in related regressive neurotic and psychotic syndromes, I have found the use of chlorpromazine and reserpine generally unsatisfactory from the long-range point of view, with a few remarkable exceptions in which patients responded very well. All those who did respond well were marked by agitation and overactivity, and these are the patients who seem most amenable to chlorpromazine therapy. Reserpine, on the other hand, was useful in some patients in phobic states. All these patients, however, had one thing in common with manic patients: while the ego boundaries had been breached by panic anxiety, any secondary paralysis of important ego functions was absent or relatively slight, the clinical picture being dominated by excitation. As might then be expected, none of the obsessive-compulsive patients was benefited at all, not even temporarily.

The great variety in the response of patients with neurotic and borderline states to tranquilizing drugs may be in part explained by the fact that one of the more important effects of these drugs is that they enhance suggestibility. West[8] has shown that the use of these drugs increases the ease with which these patients can be hypnotized or otherwise influenced by suggestion. This highlights the fact that additional therapeutic actions and/or attitudes of the physician may play a decisive role.

Chlorpromazine is useful in relieving states of excitation in the psychoses arising from chronic alcoholism and in states of pathological alcoholic intoxication[9] as well as in cases of drug addiction for relieving nervous-system excitation released by withdrawal of narcotics.[10] Both chlorpromazine and reserpine are useful in senile psychoses. In a patient with presenile sclerosis (Alzheimer's disease) with marked agitation, overactivity, and increased stream of talk, a remarkable degree of social improvement was brought about by administration of chlorpromazine. Chlorpromazine and reserpine have also been found helpful in the control of chronically disturbed patients in mental hospitals. In the majority of these patients, this method of control merely suppresses symptoms without bringing about actual recovery; however, physicians who have used large doses of reserpine in such hospital populations of persons with apparently chronic, incurable schizophrenia have consistently reported a social recovery rate of 20%, so that many such patients are able to return home after many years of hospitalization.

Other New Drugs

A number of additional new drugs have become available that differ from the tranquilizing drugs in varying degrees. I should like to divide these into three groups: (1) relaxant drugs, (2) ataraxic (deconfusing) drugs, and (3) antiphobic drugs. The action of relaxant medication, such as that exemplified by the new drug meprobamate (Miltown),[11] is similar to that of the tranquilizing drugs, except that its inhibitory effect is less profound. This is an advantage in the psychoneuroses, in which marked reduction of drive such as that brought about by tranquilizing drugs is often anxiety provoking and thus tends to counteract the desired effect of the medication. Because of its less profound inhibitory action, meprobamate also does not tend to precipitate or aggravate depression, but for the same reason it is also much less effective in the treatment of psychotic states of excitement.

Ataraxic (deconfusing) action has been described as the characteristic effect of Frenquel[12] [α-(4-piperidyl) benzhydrol hydrochloride]. In contrast to the tranquilizing drugs, Frenquel does not depress the activity of the hypothalamus either clinically or in the electroencephalogram; it counteracts the effects of lysergic acid diethylamide (LSD-25) and of mescaline without inducing sedation and restores the resting activity in the electroencephalogram after its disruption in the form of enduring arousal by lysergic acid diethylamide or mescaline.[13]

Antiphobic medication, as with Benactyzine (2-diethylaminoethyl benzilate hydrochloride), is fundamentally different from tranquilizing medication in that it selectively abolishes "neurotic" inhibitory avoidance responses engendered by stress without inhibiting the orienting response and conditional reflex responses.[14] Consistent with the conceptual scheme presented in this paper, this drug has proved itself in the hands of others[15] as well as myself to be a mild antidepressant in clinical states of depression in human beings, of both manic-depressive and involutional type. Further studies of these and related compounds promise to shed further light upon the neurophysiological and biochemical aspects of emotional and mental disorders and to aid in their treatment.

Summary

Electroshock therapy relieves the secondary traumatic state of the ego (panic and/or depression) by reducing the excitability of the nervous system, especially the cortex. Unconscious (subcortical, epinephrine-precipitable) warning anxiety can then no longer overstimulate the cortical ego and thus frighten it into panic or paralyze it into depression, as it did formerly along the lines of Pavlov's paradoxical reaction. The ego and its defenses appear strengthened after electroshock therapy, because its excitation threshold has been raised. The new tranquilizing drugs (chlorpromazine and reserpine) relieve the primary, unconscious, subcortical, epinephrine-precipitable warning and tension anxiety that impels states of excitation. They are thus capable of relieving states of agitation and overactivity, especially manic psychoses and organic-toxic states, in which secondary inhibitory or disorganizing effects upon the ego are slight or readily reversible. The action of certain newer groups of drugs, which may be classified as relaxants (such as meprobamate [Miltown]), ataraxic (deconfusing) (such as Frenquel [α-(4-piperdyl) benzhydrol hydrochloride]) and antiphobic (such as Benactyzine [2-diethylaminoethyl benzilate hydrochloride]), is different from that of the tranquilizing drugs. They require further study of their psychophysiology and clinical indications.

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CLINICAL NOTES

MEASUREMENT OF BLOOD PRESSURE IN OBESE PERSONS

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and
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The clinical measurement of arterial blood pressure by the auscultatory method is known to be subject to error. The initial technique, introduced by Riva Rocci,[1] using a 5-cm. cuff, was subsequently demonstrated to be erroneous by the investigations of Von Recklinghausen in 1901.[2] Von Recklinghausen established the clinical method for measurement of blood pressure by showing that sufficiently accurate results were obtained by means of a wider cuff. He postulated that the cuff transmits pressure directly to the artery and that this is not modified by the soft tissue, provided the soft tissue is of normal elasticity and the proper cuff width is employed. The standard 13-cm. cuff is now widely used, although falsely high blood pressures may be obtained in obese patients[3] and low values may be obtained using the 13-cm. cuff in children with small arms.[4]

The object of this study was threefold: (1) to demonstrate the error in taking blood pressure by the conventional method in subjects with large arms; (2) to investigate the accuracy of a new forearm method for measuring blood pressure; and (3) to explore the role of tissue composition as a cause of error in subjects with large arms.

Method

In the forearm method the standard 13-cm. cuff was placed on the forearm with its midpoint 13 cm. from the olecranon process, and the blood pressure was determined by either auscultating or palpating the radial artery. For comparative purposes the blood pressure was obtained in 100 persons, both by the usual method (cuff on upper arm and auscultation of brachial artery) and by the forearm technique. The circumferences of the upper and lower parts of the arm were determined by a tape measurement 13 cm. proximal and distal to the olecranon process. The pressure readings were taken in routine examination of 100 consecutive patients and staff members of a general hospital.

The brachial or radial intra-arterial pressure was determined in 14 additional persons. In eight persons there was no significant difference between the forearm and upper-arm pressure readings, and these served as a control group. Six patients had a marked discrepancy between the pressure readings at the two sites and comprised the second group. These six were originally selected because of extreme obesity. The blood pressure was determined after the patient rested either supine or sitting comfortably with the arms supported until the blood pressure reached a steady state. The circumferences were measured as already described, and numerous blood pressure readings were taken at the two sites on both arms with a standard width cuff with metal clips and a mercury manometer. An arterial needle was then introduced, after procaine hydrochloride infiltration, into the brachial or radial artery, and the arterial pulse was recorded by means of a Statham strain gauge and amplifier. At the same time, or immediately before and after, the blood pressure was determined by the cuff method in the same arm.

In order to study the role of tissue elasticity, six normotensive subjects were chosen whose blood pressure was the same in each arm. One of the upper arms was loosely wrapped with cotton to a circumference of 45 cm. The blood pressure was then taken with the 13-cm. cuff and the cuff progressively tightened, thus compressing the cotton. Serial blood pressure determinations were recorded in both arms, the opposite arm serving as a control. In six normotensive patients one upper arm was increased in size to 45 cm. with less compressible gauze wound firmly around the arm, and the blood pressure was again recorded simultaneously in both arms.

Simultaneous Measurements of Blood Pressure in Upper Arm and Forearm and Recording of Intra-Arterial Pressure

Case No.	Age, Yr.	Body Surface Area, Sq. M.	Arm Circumference, Cm.		Indirect Blood Pressure, Mm. Hg		Direct Blood Pressure, Mm. Hg
			Upper	Lower	Upper	Lower	
			Group 1*				
1	50	2.16	33	27	152/ 90	148/ 84	150/ 82
2	59	1.66	31	25	188/118	182/114	184/104
3	49	1.76	26	25	168/ 92	160/100	166/ 85
4	42	1.76	25	23	154/ 58	140/ 54	138/ 52
5	61	1.80	27	24	120/ 78	110/ 80	103/ 69
6	61	2.00	32	25	126/ 78	130/ 78	117/ 61
7	40	1.90	33	23	270/124	270/120	275/110
8	53	2.30	39	31	150/100	136/ 96	144/ 94
			Group 2†				
9	65	2.20	44	27	188/110	142/ 82	146/ 78
10	69	2.30	38	25	190/110	146/ 94	153/ 74
11	61	2.30	40	29	196/116	158/100	164/ 98
12	61	2.20	43	32	144/ 98	110/ 78	107/ 66
13	63	2.30	48	31	200/110	150/ 90	120/ 78
14	74	2.10	46	26	250/150	150/ 92	148/ 84

* Eight normal subjects who had no significant difference in blood pressure readings by the three methods.

† Six obese subjects who all had false elevation of the blood pressure measured in the upper arm.

Results

In 79 of 100 subjects there was a difference of 10 mm. Hg or less in systolic pressure taken by the standard as compared with the forearm technique. Seventeen subjects showed a difference of 10 to 20 mm. Hg, and four subjects had a difference of over 20 mm. Hg. In these four subjects the upper arms were obese, the arm circumference ranging from 28 to 36 cm. in each instance, and the pressure was always higher in the upper arm. Six subjects had muscular arms measuring over 35 cm. in circumference and yet had less than 10 mm. Hg difference between upper and forearm measurements.

The table shows the results of the intra-arterial pressure determinations and of the pressures recorded

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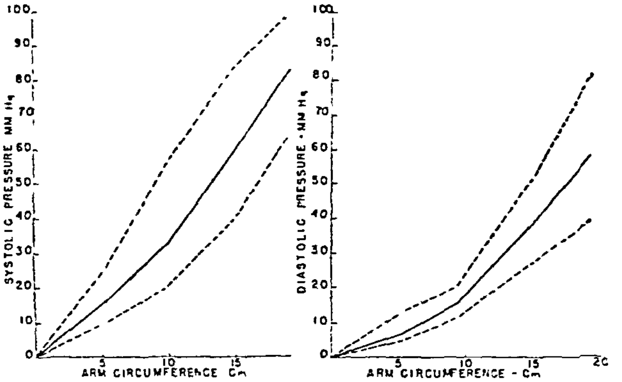
From the Cardiac Clinic, Division of Internal Medicine, and the Cardio-Respiratory Laboratory, Grasslands Hospital. Dr. Trout is now at Hillsdale, N. Y.

in the upper and lower arm with the sphygmomanometer in 14 subjects. In the patients with a difference in pressure at these two locations, the forearm pressure correlated closely with the intra-arterial pressure. In all members of this group the body surface area was 2.1 sq. m. or above and the circumference of the upper arm exceeded 38 cm. In addition, the upper arms of these six individuals were flabby and consisted, for the most part, of rolls of fatty tissue. The figure indicates the systolic and diastolic errors (artefact) encountered in the normotensive subjects whose upper arms were increased in circumference by adding compressible cotton. As the arm circumference was progressively increased with cotton, similar systolic and diastolic overshoot, or artefact, occurred. When this was repeated with the less compressible gauze there was only a negligible (5 to 8 mm. Hg) rise in pressure until the gauze became 15 to 20 cm. thick, at which point there was a 20 to 40 mm. Hg systolic error and a 20 to 30 mm. Hg diastolic error.

Comment

In 1941 Ragan and Bordley[3] demonstrated the error incurred by taking the blood pressure in large arms with the standard 13-cm. cuff. After investigating such patients with a 20-cm. cuff, they concluded that the 20-cm. cuff did not regularly increase the accuracy of the determination and was apt to give erroneously low reading, particularly in obese patients with actual hypertension. The forearm technique, herein described, appears to give accurate systolic and diastolic readings, so that it can be used when the standard technique reveals hypertension in obese persons with large flabby arms. The reasons for such falsely high pressure readings are not entirely clear.[5] The patients in the present study in whom there was a large error in upper arm readings all had flabby tissue in addition to having large upper arm circumferences. This led to the study of blood pressure readings in normal subjects made artificially obese by wrapping the arm with cotton and gauze. It would seem, from the large error introduced by the cotton as opposed to the small error produced by the gauze, that there is a loss of pressure across compressible substances that may result in falsely high readings. The finding of comparable blood pressure recordings in upper and lower arms in well-muscled individuals with large arm circumferences tends to support this hypothesis.



Left, error in systolic pressure caused by wrapping the arm under the cuff with cotton. The solid line represents the mean of results obtained in six subjects, and the broken lines are the maximum variations recorded. *Right*, error in diastolic pressure caused by increasing the arm circumference with cotton.

Summary and Conclusions

Falsely high blood pressure readings may be obtained in people with obese upper arms. In markedly obese individuals, the true arterial blood pressure may be more accurately determined by measuring blood pressure in the forearm rather than in the upper arm. Tissue composition as well as the arm circumference may contribute to the erroneously high blood pressures recorded in obese subjects.

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DIAGNOSTIC VALUE OF BULBOCAVERNOUS REFLEX

Jack Lapides, M.D.
and
John M. Bobbitt, M.D., Ann Arbor, Mich.

Difficulty in urination is often the first clinical manifestation of a lesion of the sacral part of the spinal cord. No other obvious sign or symptom may be present, since the motor defect can be too low to involve movements of the lower extremities, and the sensory deficit, if present, is in the perineal region, an area where anesthesia is not discovered readily by the patient. Even a complete physical examination might not disclose the lesion, since one ordinarily does not test for sensory deficits in the saddle area. Since obstructive uropathy is the usual cause for a decrease in size and force of stream, the patient undoubtedly would be subjected to a urologic investigation. Endoscopy and cystometry might lead to a correct diagnosis if bladder sensation were absent. However, if sensation were intact and only the motor side involved, then the diagnosis might be missed and an unnecessary prostatectomy performed.

In the child, dysfunction of the sacral part of the spinal cord is seen most commonly with spina bifida and myelomeningocele, while, in the adult, trauma, neoplasm, and herniated intervertebral disk are the usual etiological factors.

Every patient with a history of hesitancy in urination, decrease in size and force of stream, and straining to void or urinary retention should be subjected to an examination for intactness of the sacral part of the spinal cord, for the motor and sensory neurones concerned with urination are situated at sacral spinal seg-

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From the departments of surgery, University of Michigan Medical School and Veterans Administration Hospital.

ments 2, 3, and 4. The integrity of the sensory component can be ascertained by testing the saddle area for reaction to pinprick. An effective method for determining the status of the motor side involves the use of the Bors [1] modification of the bulbocavernous reflex.

When the glans penis in the normal male or the clitoris in the female is compressed firmly between thumb and index finger, reflex contraction of the bulbocavernosus and external sphincter ani muscles occurs. The shortening of the bulbocavernosus muscle is difficult to feel, whereas tightening of the anal sphincter is readily perceived by placing the index finger in the distal portion of the anal canal or the anus. Although the reflex test can be done by one individual, it is best to have two people perform the examination: one to squeeze the glans penis and the other to note the contraction of the anal sphincter. Occasionally the response is quite delicate, and one individual may not detect it if he is preoccupied with eliciting the reflex.

In order to obtain a good response of the anal sphincter, the patient must be relaxed, for the reflex contraction will not be felt if the musculature of the pelvic floor is already in a contracted state. In addition, the examiner should not compress the glans penis more frequently than once every four seconds, in order to allow the reflex arc an adequate recovery period.

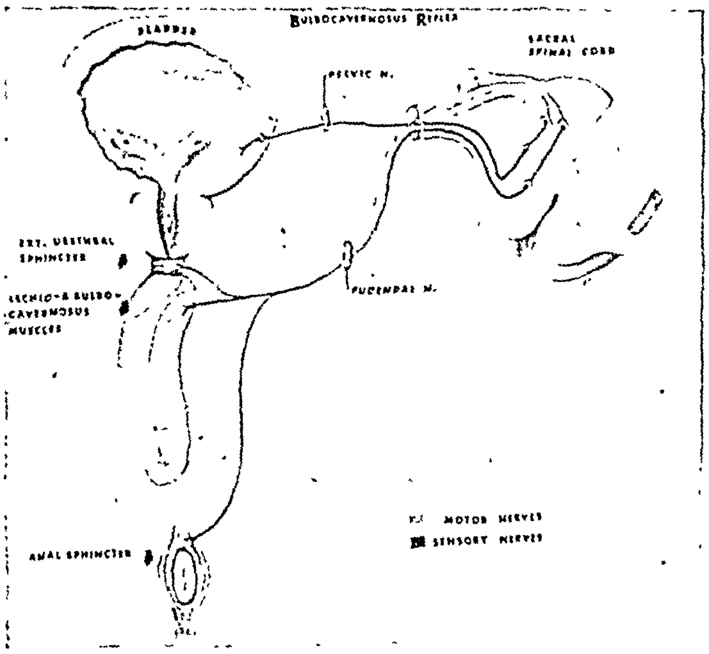

Diagram illustrating the components of the bulbocavernous reflex arc and its relationship to the innervation of the bladder.

The bulbocavernous reflex arc is depicted in the figure and is composed of fibers from the pudendal nerve. When deep pressure is applied to the glans penis or clitoris, subcutaneous Pacinian corpuscles are stimulated to send sensory nerve impulses along the dorsal nerve of the penis or clitoris to afferent neurones situated in the posterior root ganglions. These sensory neurones, in turn, stimulate (through internuncial neurones) motor neurones of the external anal sphincter and bulbocavernosus muscles. The motor impulses are transmitted along fibers of the deep perineal branch of the pudendal nerve. The synapses of the bulbocavernous reflex arc are situated in the sacral part of the spinal cord; occasionally the synapses may lie as high as L-5.[2]

The urology section at the University of Michigan Medical Center has found the bulbocavernous reflex so informative it has been incorporated as part of the routine physical studies of patients with urologic complaints. The value of the bulbocavernous reflex is demonstrated by the following two cases seen recently.

Report of Cases

CASE 1.—A 48-year-old man was referred to the Veterans Hospital with the diagnosis of prostatism and acute urinary retention. The patient related that he had noted the onset of hesitancy, dysuria, and straining to void about three weeks prior to admission. His micturitional difficulties increased gradually in severity and led to complete urinary retention the day before hospitalization. He was admitted with an inlying urethral catheter in place. Physical examination revealed a chronically ill-appearing male with multiple subcutaneous nodules. The prostate gland was normal in consistency and contour. The bulbocavernous reflex was absent; patchy saddle anesthesia was present. Cystometrography revealed a large bladder capacity with decreased exteroceptive and proprioceptive sensation; there were no uninhibited contractions, and the patient was unable to void. In view of the subcutaneous nodules and evidences of dysfunction of the sacral part of the spinal cord, a tentative diagnosis of neoplasm metastatic to skin and spinal cord was made. Endoscopy confirmed the examiner's suspicions by demonstrating no signs of obstructive uropathy. Subsequent studies disclosed bronchogenic carcinoma with extensive metastases to skin, bone, and the sacral part of the spinal cord.

CASE 2.—A 37-year-old male was admitted to the University Hospital with the complaint of intermittent low back pain present since 1944. Recently the pain had increased in severity and radiated down the right lower extremity. Physical examination was negative, except for moderate limitation of motion in the lumbosacral spine and an absent ankle jerk on the right. A diagnosis of ruptured nucleus pulposus was made, and it was decided to treat the patient conservatively with traction. On the morning of the second day of hospitalization, the patient complained of hesitancy and difficulty in urinating. Urologic consultation was requested, and examination revealed no abnormalities except for an absent bulbocavernous reflex. On the basis of this finding, myelograms were made immediately; these revealed a complete block at L-5 to S-1. An emergency laminectomy was performed, with the removal of the ruptured disk. Postoperatively the patient voided with ease. The bulbocavernous reflex response was normal within several days after operation. In this case the reflex was of utmost value in that it gave immediate objective evidence that the herniated disk was impairing the function of the sacral part of the spinal cord and was thus giving rise to urinary difficulties.

Summary

Bladder dysfunction is frequently the first sign of a lesion of the sacral part of the spinal cord. Every patient with difficulties in micturition should be examined for integrity of this part of the spinal cord. The Bors version of the bulbocavernous reflex has been found to be extremely valuable in determining abnormalities of the conus medullaris.

1313 E. Ann St. (Dr. Lapides).

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COUNCIL ON PHARMACY AND CHEMISTRY

Report to the Council

The Council has authorized publication of the following report from the Committee on Toxicology.

H. D. Kautz, M.D., *Secretary.*

The following report is a summary of the 1956 annual meeting of the Committee on Toxicology. These proceedings have been digested in order to bring to the medical profession timely reports on subjects that might not otherwise come to the readers' attention. Certain of the more important topics considered and actions taken thereon by the Committee are set forth.

Bernard E. Conley, *Secretary*
Committee on Toxicology.

ANNUAL MEETING OF THE COMMITTEE ON TOXICOLOGY

The Committee on Toxicology held its annual meeting on March 29, 1956, at the headquarters of the American Medical Association, Dr. Torald Sollmann, Chairman, presiding. In addition to the Chairman and Secretary, the following members were present: Drs. J. M. Arena, H. B. Haag, A. J. Lehman, E. Press, and Mr. J. C. Ward. In addition to headquarter's representatives, Drs. E. W. Constable, State Chemist, North Carolina; K. P. DuBois, Toxicity Laboratory, University of Chicago; and W. J. Hayes and S. W. Simmons, United States Public Health Service, attended as guests of the Committee.

Abstracted reports of some of the more important discussions and actions follow:

Kerosene Poisoning.—A subcommittee on poisoning by kerosene was appointed to study measures for improved safety in the use of petroleum distillates. Progress was reported on current projects to develop a monograph on kerosene poisoning and to promote precautionary labeling. Proposals for the clinical evaluation of various methods of treatment and laboratory investigation of methods for determining amounts of absorbed kerosene were discussed. The Committee agreed to join the American Academy of Pediatrics and the American Public Health Association in a joint clinical study of the treatment of poisoning by kerosene and petroleum distillate.

Exploitation of Nonprescription Drugs.—During the past year, several instances potentially harmful to the public health, especially that of children, have occurred. Representative situations include promotion of a clown-shaped medicine bottle designed to attract children to the container, promotion of vitamin pills on a children's program in a manner appealing to the toddler's tastes for sweets, and distribution of aspirin by vending machines. Since drugs cause 20% of the accidental deaths (33% in children under 5 years) and 22% of the suicides from nongaseous poisons, the Committee feels compelled to comment on these developments.

Devices intended to tempt children to accept drugs as something other than medication can have only unfortunate consequences. Medicine containers designed as toys tempt the very young to take freely of their contents. Vending machines for the automatic dispensings of aspirin, vitamins, and other nonprescription drugs are subject to the same censure. Such machines operate unattended, and children cannot be expected to discriminate between those that dispense gum and candy and those that dispense drugs. Accordingly, the Committee moved that it be placed on record as against the use of vending machines for drugs in public places accessible to children and others lacking in mature judgment.

Poison: Definition and List.—The Committee has been repeatedly asked to define and enumerate substances that it considers poisonous. To this end, definitions of poison presented in 11 current textbooks on pharmacology and medical jurisprudence submitted by 25 leading pharmacologists and representative legal definitions of 16 national and local government agencies in this country and abroad were collected and examined.

There is no uniformity of legal or scientific opinion as to what constitutes a poison. Various laws, both state and national, vary widely in their definitions. Statutes that employ dosage values vary in their specifications from 5 grains to 5 gm. as the "destructive," "deadly," or "fatal" quantity for "(adult) human life." Those state laws not utilizing a quantitative definition employ vague, indefinite, and generally unsatisfactory terms such as "noxious," "deleterious," or "virulent poisons" to specific chemicals classed as poisons.

Since a precise definition that would fit all circumstances is not possible, the Committee felt that any substance that, when improperly used, may produce harm by chemical action should be provided with an appropriate precautionary label statement. Such precautionary statements should provide warnings for different categories of hazards.

A list of several hundred poisonous substances compiled from legal and trade sources in this country and abroad is also under consideration for adoption.

Public Education About Poisons.—A report of a conference between a Committee representative and school health workers in Richmond, Va., was given regarding means for education of the public about poisons. The school health workers felt that a variety of approaches should be used, such as poster contests on chemical safety and distribution of pamphlets similar to those given away during Fire Prevention Week. They felt that the 30 million school children could be made watchdogs for chemical safety.

The value of radio and television programs presented in such form as to be appealing to both children and parents was stressed. Local chapters of the American Red Cross and the Parent-Teacher Associa-

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION
Edited Under the Direction of the Board of Trustees

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Subscription price . . Fifteen dollars per annum in advance
Cable Address . . . . "Medic, Chicago"

PROGRESS REPORT OF AMERICAN DIABETES ASSOCIATION ON ORALLY EFFECTIVE HYPOGLYCEMIC SULFONYLUREAS

GUEST EDITORIAL

Arthur R. Colwell, M.D.
Dwight Ingle, Ph.D.
Maurice E. Krahl, Ph.D.
Rachmiel Levine, M.D.
and
Henry T. Ricketts, M.D.

Almost a year has elapsed since the beginning of the current revival of interest in the sulfonylureas as hypoglycemic agents. The first announcements, made in the German medical press in October, 1955,[1] were quickly relayed to other countries, including Canada and the United States. Intensive study is being conducted here and the sale of the drugs is being postponed pending substantial proof of safety in prolonged use, mechanisms of action, and clear indications for therapy. Two pharmaceutical firms are supplying their products, now known as carbutamide (BZ-55) and tolbutamide (Orinase, U-2043), to clinical investigators who are observing their action in many laboratories and in several thousand diabetic subjects.

Three conferences have been held during 1956 (two in Indianapolis and one in Kalamazoo) in which leading researchers in the United States and Canada have reported current data and debated their significance. Symposiums on the subject have been or will be published in current issues of several medical journals.[2] The intensity and caution with which the developmental work has been conducted here can well serve as a model for products of this nature. It is reminiscent of the care with which insulin itself was studied before general release. The evidence in support of current concepts concerning mechanisms of action and clinical use of these compounds cannot be reviewed in a brief editorial report such as this. Interested readers are referred to the mass of data already or soon to be reported.[2]

The compounds do not appear to increase utilization of glucose by the peripheral tissues. Early suggestions that the liver might be the major site of action have not received convincing support, although the output of glucose from the intact organ does seem to be reduced. With larger than therapeutic doses, thyroid hyperplasia results from chronic use of carbutamide in animals and radioiodine uptake is reduced in man, but these appear to be side-effects, as with thiourea compounds. There seem to be no measurable effects of the new drugs on anterior pituitary or adrenocortical function.

At present the best estimate as to the site of action points to the pancreas. The early German studies suggesting alpha-cell destruction with inhibition of glucagon production have not been confirmed. On the other hand, an effect dependent on the presence of beta cells is strongly suggested by almost uniform lack of response to the drugs in alloxanized subjects and those who have undergone total pancreatectomy and in "total" spontaneous diabetes, especially in juveniles. An effect on beta cells to cause release of insulin is indicated by studies on direct pancreatic perfusion, cross circulation, and islet size, but the fact that certain physiological actions of the compounds are unlike those of insulin casts some doubt upon this hypothesis. Insulin itself inhibits ketosis, enhances the peripheral utilization of glucose, increases the glycogen content of muscle, and raises the blood pyruvate level. At the moment it is not clear whether sulfonylurea action is accompanied by such criteria of insulin effects.[2c] Data of different investigators are conflicting on this point. This may be due to the manner by which the drugs affect insulin secretion, or possibly we are dealing with the release of hypoglycemic agents other than insulin.

Members, American Diabetes Association Informational Committee on Antidiabetic Compounds (Chairman, Dr. Colwell).

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Therapeutically the compounds reduce hyperglycemia and glycosuria in many persons with mild and early diabetes. They are virtually ineffective in severe forms of the disorder where insulin-dependence is manifest. The diabetics likely to respond best are those who need insulin the least, as a rule. For this reason they may be the very same patients who should restrict food intake, lose weight, and conserve natural islet function, and not receive help from drugs. There are hints that beta-cell exhaustion may follow long-continued use of the drugs—an additional reason for the utmost caution in their wide application.

Toxic reactions to carbutamide seem to be on the order of those seen with other sulfonamide compounds. A recent survey shows severe hematological, hepatic, and generalized allergic reactions in about 2% of some 7,000 patients and milder side-effects, such as skin rashes and gastrointestinal symptoms, in an additional 3%.[2d] In another study the incidence of side-effects in 279 cases was about 9%.[2d] There have been a number of fatalities.[2d] No similar objective data are available yet on tolbutamide. Maintenance dosages of about 1 gm. daily and blood levels in the range of 10 to 15 mg. per 100 ml. appear to be effective and safe in most instances, but it must be borne in mind that allergic reactions may occur with much smaller amounts.

The usefulness of these drugs probably will be limited to those diabetics who do not really need insulin. In some cases these drugs will be useful, also, to those who refuse to take insulin, who are allergic to it, or who should not take it because of occupational hazards.

THE PHYSICIAN AND DISASTER

Recent natural disasters occurring in the United States and abroad once again serve as a reminder to the practicing physician of his responsibilities to the community, over and above the immediate care of his patients. After floods, hurricanes, tornadoes, fires, and lightning and vehicular accidents, the public, besieged with reports of what has been done to bring calm out of chaos, is rarely told how to prepare for similar future calamities. At an even later date, the medical journals come forth with preventive medical programs for the protection of food supplies, sanitation procedures, and evacuation techniques based on past experience, but mainly directed at the public health facilities of an area.

What of the private practitioner? Where does he find out what to do when the next disaster strikes? Nothing in the medical literature or in the wealth of civil defense material can make him part of a planned disaster service team while he is sitting in his office or making home and hospital calls. Also rare is the medical society whose disaster plan is so complete that members not only know their duties but have even had trial or practical examples.

Much of the so-called medical unpreparedness has been blamed on lethargy and disinterest, along with multitudes of other excuses. The situation is analogous to the disease that has many purported cures—no one really knows the answer. Today's community physician would gladly give of his time and effort if he only knew when, where, and how his particular services were actually needed. It cannot be called unusual that many a well-intentioned physician has voluntarily proceeded, or has been directed, to some disaster scene only to find the situation completely under control and half a dozen more of his colleagues standing around knowing they were not needed but unable to leave due to conceivable public reaction, or the remote possibility of their services being required at a later time.

What appears to be necessary in the event of most natural disasters is a type of medical aid program planned and sponsored by the local medical society. This should be based on a particular community's needs and fully coordinated with local health, police, and other disaster officials. As only one example, a society forms a panel of four or more physicians who would usually be available when the need arose. If and when medical aid is called for, the number-one physician on the roster will be contacted (or number two if the first cannot be reached) and escorted to the disaster scene. This physician then would assume the responsibility of requesting and securing additional selected medical personnel if actually required or alerting hospitals and other medical care facilities to have medical aid waiting for casualties to arrive. Much better care can be afforded patients where proper equipment exists and where no one hospital receives more than it can properly handle. An example of another type of program is given on page 985 of this issue.

Naturally there are many ways to obtain the same successful medical disaster plan, but it appears that to achieve any result the leadership must be in the hands of those who are actually to perform the service. Of course, cooperation between adjacent communities will have to be organized, but this should be secondary to taking care of one's own. Integrating a locally devised, practical disaster plan with state and national civil defense would perhaps be more workable than directing the medical profession "from above" without regard to cultural patterns and existing resources. A compendium of the best local ideas could then be adapted to a nationwide plan.

ORGANIZATION SECTION

REPORT OF JOINT COMMISSION ON ACCREDITATION OF HOSPITALS

The August, 1956, bulletin of the Joint Commission on Accreditation of Hospitals (660 N. Rush St., Chicago: Kenneth B. Babcock, M.D., director) is reproduced below for the information it contains that will be of interest to many physicians.—Ed.

A meeting of the Board of Commissioners of the Joint Commission on Accreditation of Hospitals was held on July 28, 1956 in Chicago. Raymond Peterson, M.D. was welcomed as a new Commissioner. Dr. Peterson represents the American Medical Association and was appointed to serve the unexpired term of the late Rolland J. Whitacre, M.D.

"Stover" Report

The Commissioners representing the American Medical Association presented the report of the Committee of the American Medical Association House of Delegates to Review the Functions of the Joint Commission on Accreditation of Hospitals. This report was approved by the House of Delegates in June, 1956.

CONCLUSIONS OF THE COMMITTEE

1. *Accreditation of hospitals should be continued.*
2. *The Joint Commission should maintain its present organizational representation.*
3. *The Board of Trustees should report annually to the House of Delegates on the activities of the Joint Commission.*
4. *Physicians should be on the administrative bodies of hospitals.*

The Board of Commissioners reviewed the report carefully and expressed on record that Wendell C. Stover, M.D., Chairman, and his committee had conducted an objective study of the functions of the Commission and that the report of their findings was judicious and statesmen-like.

Because we would like to share this excellent and important report with you, a copy is enclosed. It is complete except for a reproduction of the "Standards for Hospital Accreditation", the names of the Commissioners, and the corporate structure of the Commission which were included in the original report. The reference committee of the Council on Medical Education and Hospitals of the American Medical Association added a single recommendation urging the Commission to study "the problem of the exclusion from hospitals and arbitrary limitation of the hospital privileges of the general practitioner" and to seek methods whereby hospital privileges can be determined and granted "on the basis of professional qualifications and demonstrated ability."

In order to understand the actions of the Board of Commissioners, we urge that you read the "Stover" report first. We would also like to solicit your help in extending this information as widely as possible by sharing this Bulletin with your staff and associates.

ACTIONS OF THE BOARD OF COMMISSIONERS

1. Agreement.
2. Agreement.
3. No action by the Board of Commissioners indicated.
4. Very close liaison between the medical staff and the governing board of a hospital must be maintained. The method used to accomplish this should be determined locally.

   By way of explanation, the Commissioners think that the composition of the governing board of a hospital should be determined at the local level and that the Commission should not specifically state whether physicians should or should not be members. From its inception, the Commission through its publications has stated that in accredited hospitals close liaison between the medical staff and the governing board is essential. To assure good quality patient care, good working relationships are vital. However, the selection of the most effective way to accomplish this goal in the individual hospital can best be determined locally.

   We call your attention to the recommendations made in June, 1953 by the Joint Committee of the Boards of Trustees of the American Medical Association and the American Hospital Association on Hospital-Physician Relationships. We quote as follows—

   > "The general purpose of hospitals and physicians is to aid each other in the delivery of the best possible medical care to patients. To attain such a purpose requires full cooperation among medical staffs, governing boards and administrative heads of hospitals. One important method of attaining this objective is that duly designated representatives of the medical staff shall have full and direct access to the governing board with due consideration to the position of the administrator as chief executive officer of the hospital. The various methods by which the medical staff may have access to the hospital governing board follow. These methods are not listed in the order of their desirability, and there may be other acceptable liaison plans developed depending upon local conditions.

a. The executive committee of the medical staff and a committee of the governing board with the hospital administrator can serve as a joint committee.

b. Representatives of the medical staff can serve as members of the medical staff committee of the governing board with the hospital administrator.

c. Representatives elected by the medical staff can attend meetings of the hospital governing board.

d. Members of the medical staff can be members of the hospital governing board."

To repeat, the Standards for Hospital Accreditation state that the "governing body . . . should . . . establish a formal means of liaison with the medical staff preferably by a joint conference committee" (a or b above); however any one or combination of the above methods that prove effective are acceptable.

5. *General practice sections in hospitals should be encouraged.*	5. The present policy of the Commission with respect to general practice sections should be continued, that the decision as to the establishment of a general practice department should be made by the local medical staff.
6. *Staff meetings required by the Joint Commission are acceptable, but attendance requirements should be set up locally and not by the Commission.*	6. Referred to a committee for study; a report and recommendations to be submitted at the next meeting of the Board of Commissioners to be held in December, 1956. Since this Conclusion constitutes a change in the Standards, the established procedure for changing standards was followed. In April, 1954, the Commissioners voted that the following procedure for changing the Standards for Hospital Accreditation be adopted: "Any proposal for a change, addition or deletion in the Standards for Hospital Accreditation of the Joint Commission on Accreditation of Hospitals shall be presented and discussed at a regular meeting of the Board of Commissioners. A committee shall then be appointed to submit recommendations at the next regular meeting of the Board of Commissioners. If agreement to the proposed change is unanimous among those present and voting, the proposal will be adopted. If there is one or more dissenting votes, action will be deferred until the next meeting of the Board, at which time a majority vote will be decisive."
7. *The Joint Commission should not concern itself with the number of hospital staffs to which a physician may belong.*	7. The Standards for Hospital Accreditation do not restrict multiple staff appointments.
8. *The Joint Commission is not and should not be punitive.*	8. Agreement.
9. *The Joint Commission should publicize the method of appeal to hospitals that fail to receive accreditation.*	9. In the event a hospital is not accredited following a survey, the process of appeal will be explained in the letter notifying the hospital that it has not been accredited. The original Bylaws of the Joint Commission on Accreditation of Hospitals in Article III, Section 8 provide for such hearings. A copy of the Bylaws was distributed with the first issue of the Bulletin of the Commission in November, 1952.
10. *Reports on surveys should be sent to both administrator and chief of staff of hospitals.*	10. Copies of the covering letter and recommendations sent to the administrator following a survey will also be sent to the chief or president of the medical staff and the president of the governing board.
11. *Surveyors should be directly employed and supervised by the Joint Commission.*	11. There is no objection in principle that surveyors could be directly employed and supervised by the Commission. Whether or not this is done is a decision for each member organization of the Commission to make.
12. *Surveyors should work with both administrator and staff.*	12. Agreement.
13. *New surveyors should receive better indoctrination.*	13. The orientation program for surveyors is being steadily strengthened.
14. *Blue Cross and other associations should be requested not to suspend full benefits to nonaccredited hospitals until those so requesting have been inspected.*	14. Pertains to individual Blue Cross Plans and cannot be acted upon by the Joint Commission on Accreditation of Hospitals.
15. *The American Medical Association should conduct an educational campaign for doctors relative to the functions and operations of the Joint Commission.*	15. No action.

16. *The Committee also suggests that the American Medical Association and the American Hospital Association encourage educational meetings for hospital boards of trustees and administrators either on a state or national level to acquaint these bodies with the functions of accreditation.*

17. *This Committee asks to be discharged upon submission of this report to the House of Delegates.*

16. No action.
Although it is inappropriate for the Commission to take action on Conclusions 15 and 16, the Commission will actively support the member organizations in accomplishing these objectives.

17. No action.

Change in Published List of Accredited Hospitals

In publishing the annual list of accredited hospitals, the practice has been to separate the fully accredited and provisionally accredited hospitals. These designations have been used for many years and the attitude has developed that provisional accreditation implies a secondary type of accreditation. This attitude is incorrect. The Commission has interpreted provisional accreditation to mean that a hospital meets the Standards for Accreditation to a degree that recognition should be given and that the potentialities for full accreditation exist. To avoid perpetuating a misunderstanding, hospitals will now be accredited for one year or for three years. In the annual published list no distinction will be made between hospitals accredited for three years and those accredited for one year.

Except for the publication of the annual list, there are no other changes in policy or administrative procedure. Accreditation for three years applies to those hospitals now fully accredited and accreditation for one year applies to those now provisionally accredited. Following a survey, the hospital will be informed of the period of time for which it is accredited. Those accredited for one year will be visited the following year. If on the second successive survey the hospital is again accredited for one year, it will be notified that following the third survey it must have improved patient care to warrant three year accreditation or be reduced to non-accreditation.

Certificates of Accreditation will be issued only to those hospitals accredited for three years.

Accreditation of Psychiatric Hospitals

The Board of Commissioners considered the program of accreditation of psychiatric hospitals. Daniel Blain, M.D., Medical Director, American Psychiatric Association, and Raymond W. Waggoner, M.D., Member, Central Inspection Board of the American Psychiatric Association, were invited to participate in the discussion. It was decided that a committee of the Board of Commissioners would request a meeting with representatives of the American Psychiatric Association to discuss the program further and submit a report at the next meeting of the Board of Commissioners.

PUBLICATIONS ON INDUSTRIAL HEALTH AVAILABLE

The Council on Industrial Health, American Medical Association, 535 N. Dearborn St., Chicago 10, announces the availability of two publications. "Absence from Work Due to Non-Occupational Illness and Injury" has been taken from the proceedings of the session on work absence of the Annual Congress on Industrial Health held in January, 1956. The publication is the work of the Committee on Medical Care for Industrial Workers, a joint committee of the Council on Industrial Health and the Council on Medical Service of the American Medical Association. It contains the statements of 22 representatives of the medical profession, management, and labor who participated in panel discussions entitled: "Where Are We?" "What Are We Doing?" "What Can We Do?" and "How Can We Make Better Use of Records?" Single copies are available without charge from the Committee on Medical Care for Industrial Workers. Additional copies are 50 cents each through the Order Department of the American Medical Association.

"Guiding Principles of Medical Examinations in Industry" has been reprinted from THE JOURNAL, July 7, 1956. Single copies will be furnished without charge by the Council on Industrial Health. Requests for multiple copies should be addressed to the Order Department, American Medical Association. Purchase orders or checks with orders will facilitate handling. The price scale is as follows: 2 to 25 copies, 6 cents each; 26 to 50 copies, 5½ cents each; 51 to 100 copies, 5 cents each; 101 to 200 copies, 4½ cents each; additional hundreds up to 1,000, $4.40 per hundred; and additional thousands, $44 per thousand.

FIRST FILM IN "MEDICINE AND THE LAW" SERIES

The role of the medical expert witness is the theme of the first of a film series on medicine and the law being produced by the Wm. S. Merrell Company of Cincinnati in cooperation with the American Medical Association and the American Bar Association. Entitled "The Medical Witness," this 30-minute film illustrates what doctors should and should not do when testifying in court. Its primary purpose is to teach doctors and lawyers how to present cases requiring expert medical testimony thoroughly and accurately so that a just decision can be made. C. Joseph Stetler, Director of the A. M. A. Law Department, stated that the need for educating doctors in courtroom technique is borne out by the fact that between 60 and 85% of all court cases involve medical testimony and require physicians as witnesses. The Law Department is assisting in the supervision of the filming of the series. This motion picture will be premiered Tuesday, Nov. 27, at the A. M. A. Clinical Session in Seattle. Prints will be available for showings at state and county medical society meetings through the A. M. A. Film Library after Dec. 15.

COUNCIL ON MEDICAL SERVICE

A STUDY OF MATERNAL MORTALITY COMMITTEES

This is part 4 of a series of articles by the Committee on Maternal and Child Care of the Council on Medical Service reviewing the organization and operation of maternal mortality study committees. The purpose of this specific study is to obtain information that may be utilized in the preparation of guides and, in turn, may be helpful in the development and operation of maternal mortality committees in other areas of the United States. The descriptive material to follow is concerned with the Maternal Welfare Committee of the Illinois State Medical Society.

Downstate Illinois Maternal Mortality Study

History.—The Maternal Welfare Committee of the Illinois State Medical Society is a long-established committee that has continuously promoted improvements in maternity care. Some of its early work included publication of pamphlets, such as "Advice to Expectant Mothers" and "What Price Abortions?" which were distributed widely by the committee under the seal of the Illinois State Medical Society. In addition to these early efforts toward improving lay education, the committee, in cooperation with the Illinois Department of Public Health and the departments of obstetrics and gynecology of the University of Illinois and the other medical colleges, participated in postgraduate professional education for improving maternity care throughout the state. The educational program consisted of lectures to county medical societies by speakers from the various universities and from the committee. A visual education program was developed at the University of Illinois to which its department of obstetrics and gynecology contributed space and facilities and the part-time services of its department personnel. This program involved the annual production of an exhibit to be shown first as a part of the scientific exhibit of the state medical society and secondly at the annual meeting of the American Medical Association. The exhibits were then returned to the university for use in undergraduate and postgraduate teaching.

The exhibits were demonstrated personally throughout the meetings by the professor of obstetrics, who was thus available for consultation to physicians attending the meetings. The exhibits were photographed, and lantern slides were made for use in undergraduate teaching at the university and in county medical society meetings. Twenty-four such exhibits have been produced, covering practically all phases of obstetrics. Photographs of the exhibit material, mounted on five 3-by-5-ft. panels, have been circulated to hospitals in the downstate area for study by physicians, nurses, and house staffs. Refresher courses were offered at the university during the summer months, and lectures were given by members of the four university medical schools as well as clinical demonstrations by the staff of the University of Illinois.

One of the valued programs in Illinois, developed by the Illinois Department of Public Health with the assistance of the department of obstetrics and gynecology of the University of Illinois and approved by the Illinois State Medical Society and the U. S. Children's Bureau, has been the inspection and licensing of hospitals. All hospitals giving maternity service are required by statute to be licensed and must comply with the regulations that were initially established by the passage of the Maternity Hospital Licensing Act of June 24, 1915. In the latest revision of this act, on July 1, 1953, the required regulations became a part of a General Hospital Licensing Act, administered by the Bureau of Hospitals. Among the requirements are acceptable records; for example, each hospital must submit to the Bureau of Hospitals a monthly report that shows the number of mothers and infants cared for, the types of delivery, operative procedures employed, the incidence and types of complications encountered, the frequency of abortions and ectopic gestation, and the number and causes of stillbirths and neonatal and maternal deaths. All hospitals at the end of each year are sent copies of their cumulative individual tabulations with those of their birth group and the entire state average. Much information of interest to the obstetric specialty is found in these statistical reports, and many hospitals make use of these data in their staff discussions and medical audit.

As early as 1937, the Maternal Welfare Committee recommended to the state medical society the appointment of county maternal and child health committees to study all maternal, infant, and fetal deaths occurring in their counties. In 1947, a program was prepared by the Division of Maternal and Child Health of the state health department and presented to the Maternal Welfare Committee and to the council of the state medical society. This program called for a thorough analysis of each death associated with gestation occurring in the hospitals outside of Chicago; it was approved by the committee and the state society and went into operation in January, 1948. (This maternal death study was exclusive of Chicago, where the subcommittee on maternal mortality of the Joint Maternal Welfare Committee of Cook County has been actively engaged in such a study since 1938.) Although improvements had been made in the maternal death rate in Illinois prior to 1948, information concerning maternal deaths was limited to that given on death certificates. It was believed that greater progress could be made in maternal care by differentiating each maternal death as to obstetric and nonobstetric causes; through a thorough appraisal of prenatal care; and by a determination of sequence of symptoms, thoroughness of laboratory studies, adequacy of consultation, correctness of diagnosis, method of treatment, autopsy findings, and questions of preventability and responsibility. The objective, then, of this joint project was to broaden knowledge of factors responsible for deaths associated with gestation, to effect a reduction of those factors, and, thereby, to effect a lower rate of maternal mortality and morbidity in Illinois.

Members.—The Maternal Welfare Committee is composed of a member and an alternate from each of the 11 councilor districts in Illinois. Appointments are made annually by the society president upon the recommendation of the councilor of each district and the chairman of the committee. The consultant in maternity and the chief of the Bureau of Maternal and Child Health are ex officio members. Two visiting obstetricians have been appointed by the committee to investigate each maternal death occurring in Illinois (exclusive of Chicago). The chairman of the committee is appointed by the president of the state medical society, and a vice-chairman is chosen by the chairman.

Scope of Study.—All deaths in Illinois (exclusive of Chicago) associated with pregnancy and three months post partum are studied by this committee. The three-month postpartum period is specified because the first three years of the study indicated no deaths over three months post partum that were classified as maternal (obstetric) by the committee. However, any death definitely related to or caused by a previous pregnancy is included in the study. A death is classified as maternal (obstetric) if it is due to such causes as hemorrhage, toxemia, and infection (puerperal, abortion, or ectopic) or to such other causes as embolism, anesthesia, shock, acute heart failure resulting from improper management of the patient, cerebral hemorrhage coincident with the delivery, and incompatible blood as well as other causes related directly to the pregnancy, delivery, or postpartum complications. Nonmaternal (nonobstetric) deaths are those that the committee feels are not related to the pregnancy, such as appendicitis; auto accidents; brain abscesses; burns; cancer; such infections as encephalitis, poliomyelitis, and pneumonia; and those that are due primarily to a preexisting disease, such as rheumatic heart disease or kidney disease. At times the committee finds it difficult to classify a death as either maternal or nonmaternal because of some preexisting disease that might not have caused the death of the pregnant woman or resulted in postpartum complications had conditions and treatment been ideal. In such cases, judgment on the part of the committee members is the deciding factor in the classification. Deaths of nonresidents are studied in the same manner and charged to the place of occurrence. They are not included in the final maternal mortality rate based on residence for that particular year but are reallocated to their state. Isolated studies of neonatal deaths in certain counties have been conducted by the chairman and certain members of the committee but have not been on a continuing basis (except in Chicago).

Operation: Agencies and Personnel Involved.—The maternal mortality study in downstate Illinois is a joint project of the Bureau of Maternal and Child Health of the state department of public health and the Maternal Welfare Committee of the state medical society. The department of public health shares the major expense in the study; it pays the travel expense of the obstetrician-investigator plus $25 per case investigated. It also handles all clerical, stenographic, and secretarial work, in addition to providing an office secretary and office space for the project. The state medical society pays the expense, including travel expense, of the committee meetings. In addition, the health department pays for the autopsy, performed by a member of the Illinois Pathological Society, if such services are otherwise not available to the attending physician.

The Bureau of Maternal and Child Health has had three sources from which to obtain information. First, a "Report of Maternal Death Form" is supplied each hospital in the state (exclusive of Chicago). The bureau requests that each hospital send this completed report to the department of public health immediately after any death associated with pregnancy (including abortion and extrauterine gestation), whether the patient died in the obstetric division or in any other department of the hospital. This report form identifies the patient and the hospital and gives the date of death; age at death; gravidity details; period of gestation; whether the death occurred before, during, or after labor; and whether it was an operative delivery. It requests information on the autopsy, primary and contributing causes of the death, and the name of the attending physician. On receipt of this report form, the office secretary for the committee's maternal death study forwards this information to the obstetrician-investigator for his follow-up.

In the event that the hospital fails to send the department of public health this special report on a maternal death, it is discovered in the monthly report previously mentioned, which, by law, must be submitted to the Bureau of Hospitals. Maternal deaths in this monthly report are checked against those special report forms that the Bureau of Maternal and Child Health is supposed to receive immediately after each maternal death. As a third check, to make sure that all maternal deaths are discovered, the bureau screens monthly all the death certificates of women of child-bearing age. If a death appears to be related in some way to a pregnancy, whether or not pregnancy was mentioned on a death certificate, the case is checked.

After the obstetrician-investigator receives the data on the death, he visits the physician who attended the patient and the hospital in which the death occurred. This visit is usually at least a month after the death, to assure that the hospital chart will have been completed and that pathological reports and all other pertinent data about the case will be available. After the inauguration of the study in 1948, a consultant in maternity (a board-certified specialist in obstetrics and gynecology and emeritus associate professor, University of Illinois) to the Illinois Department of Public Health performed this investigative task. However, during the last two years, this work has been performed by two privately practicing specialists in obstetrics and gynecology appointed by the committee. The obstetrician-investigator makes every effort to talk with the attending physician and obtain complete details on the case from him. The six-page detailed questionnaire requires a careful check of the hospital records. Occasionally it is necessary to consult with other hospital personnel and the family; this is done at the discretion of the attending physician. After completion of his study, the obstetrician-investigator makes an abstract of the case and distributes a copy to each member of the Maternal Welfare Committee prior to its meeting. All physicians and hospitals in the state are aware of the study, and, therefore, the obstetrician-investigator encounters little opposition in his quest for information on maternal deaths. The Maternal Welfare Committee, through its members in each councilor district, publicizes the activities of the committee at county society meetings and to hospital staffs, thereby laying the groundwork for a good working relationship.

All protocols of death studies that the committee members use are anonymous. Physician, patient, and hospital names do not appear; this information is known only to the obstetrician-investigator and the secretary at the Bureau of Maternal and Child Health. The full Maternal Welfare Committee meets four times a year and devotes a full day (usually a Sunday) to an audit of the protocols previously sent to the members by the Bureau of Maternal and Child Health. Although any interested physician may attend a committee meeting on request, it is not common that one does. If a regular member does not attend a meeting, he is responsible for getting his alternate to attend. At each meeting, during which an average of 20 protocols are reviewed, the chairman calls on each member to present a case. Even though the members have all had the protocols for study prior to the meeting, the case abstract is read completely. If the obstetrician-investigator, who is always present at the meetings, has further information than that which is contained in the protocol, he presents it. He also presents his impression of the hospital, as to its facilities and services, in the particular case under review. Discussion follows, and the committee decides the apparent cause of death, whether it was a maternal or a nonmaternal death, and whether it was preventable (based upon the ideal). If it is not clearly a case of unquestionable preventability, it is classified as a case with preventable factors or as not preventable. If it is classified as a case with preventable factors, such factors are listed. In the case either of a preventable death or of a death with preventable factors, the responsibility for that death is assigned to the physician, the patient, the hospital, or any combination of these. Special note is made as to whether the cause as determined by the committee is the same as that which appeared on the death certificate. A list is compiled of those procedures or specific techniques that might have been used to better advantage than those that were used by the attending physician.

After each meeting a form letter is sent from the Bureau of Maternal and Child Health to each attending physician who had a case that was discussed at the meeting. He is informed that his case was presented and asked if he wishes to have the findings and recommendations of the committee sent to him. He is given the case number and asked to write to the chairman for this information. On the physician's request, a letter is written to him pointing out the findings of the committee and their recommendations in cases similar to it. The physician is also invited to attend the next meeting of the committee to further discuss the case.

Follow-Up.—If the attending physician does not specifically indicate through written request or through the obstetrician-investigator that he desires the findings of the committee after discussion of the case, there is no other way for him to be apprised of the committee's decision in his particular case. No other person in the hospital or on the obstetric staff is given any information as to the committee's findings.

The first three-year report of maternal mortality in downstate Illinois, for the period 1948-1950, was read before the Section on Obstetrics and Gynecology at the 100th Annual Meeting of the American Medical Association in Atlantic City, N. J., June 15, 1951, and published in THE JOURNAL.[1] A four-year report was made in the *American Journal of Obstetrics and Gynecology* in 1952.[2] Also, a report of the maternal mortality study in Illinois was presented before the American Public Health Association, Maternal and Child Health Section, at the 80th annual meeting in Cleveland, Ohio, Oct. 23, 1952.

Each year the Maternal Welfare Committee submits to the Illinois State Medical Society its annual report. Results of the study, too, are used in the teaching of obstetrics and gynecology at the University of Illinois and at the University of Chicago Medical School. This material, however, is kept anonymous, so that there will be no possible connection between the case presented and the physician, hospital, or patient concerned. The Maternal Welfare Committee has had exhibits at the annual meetings of the state medical society and has stimulated interest among the obstetricians and general practitioners interested in obstetrics in the American congresses, which are sponsored by the American Committee on Maternal Welfare and held every three years.

Another service that the Maternal Welfare Committee provides in cooperation with the Illinois Department of Public Health is the furnishing of exhibits to hospitals in the state. This program of exhibiting in hospitals is a perpetual one—one exhibit in a strategic place in the hospital for two or three weeks during the year alternating with other exhibits at various times of the year, in order that each hospital in the state will have had an opportunity for its staff to become acquainted with the various complications of pregnancy and how to meet those complications. Twelve exhibits presently in use in Illinois are as follows: (1) Pregnancy in the Bicornuate Uterus, (2) Breech Presentation, (3) Uterine Carcinoma, (4) Cesarean Section, (5) Destructive Operations, (6) Ectopic Pregnancies, (7) Forceps Delivery, (8) Hemorrhage in Pregnancy, (9) Motherhood, (10) Puerperal Sepsis, (11) Toxemias of Pregnancy, and (12) Abortion. As a part of the committee's educational program, an annual report on the activities of the committee is made to the state obstetric and gynecologic society. Further presentations are anticipated for various publications.

Results: Statistical Analysis.—Prior to the inauguration of the study of maternal deaths in Illinois, a statistical study of maternal mortality in Illinois hospitals for the period 1943-1947 indicated that the mortality in 1943 was 2.07 per 1,000 live births. This was reduced to 0.98 [illegible] 000 live births by 1947.

made annually by the society president upon the recommendation of the councilor of each district and the chairman of the committee. The consultant in maternity and the chief of the Bureau of Maternal and Child Health are ex officio members. Two visiting obstetricians have been appointed by the committee to investigate each maternal death occurring in Illinois (exclusive of Chicago). The chairman of the committee is appointed by the president of the state medical society, and a vice-chairman is chosen by the chairman.

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The committee believes that the profession must be continually on the alert, in order that gains already made will not be lost and that further reduction in mortality and morbidity in Illinois can be made. The committee further believes that more widespread and earnest establishment of such study programs as it has conducted in downstate Illinois and the search for other avenues of approach taught by the findings of such a study will lead to a definite saving of lives of mothers and newborn infants.

References

1. Newberger, C.: Maternal Mortality in Downstate Illinois from 1948 to 1950, J. A. M. A. **149**: 328-330 (May 24) 1952.
2. Newberger, C.: Maternal Mortality in Downstate Illinois, Transactions of the Fifth American Congress on Obstetrics and Gynecology, Am. J. Obst. & Gynec. **64A**: 203-213 (Dec.) 1952.

Neurologic Eye Disease.—The human eye is actually a portion of the central nervous system. As the embryo grows a portion of the brain becomes more or less separated and comes to lie on the surface of the organism. This delicate and most important special sense organ is exposed to the environment and all of its accompanying dangers. . . . A number of diseases that affect the nervous system also affect the eye. Multiple sclerosis is one of the best examples. Other disorders of the brain, such as tumors, affect the eye in an indirect manner, resulting from the fact that the visual pathways may become secondarily involved. . . . The fact that the eye is often involved in this manner is of great help to the neurologist and the neurosurgeon in detecting the presence and locating the position of disorders of the brain. Many brain tumors first manifest themselves by alterations of vision in one or both eyes, and by careful study of such alterations it is often possible to locate the trouble accurately and at times to predict the exact type of difficulty. . . . Pituitary tumors are one of the most frequent neurologic conditions producing loss of vision. This results from the close proximity of the pituitary gland to the optic chiasm or crossing point of the two optic nerves. Loss of vision is usually the first and only symptom of these tumors. . . . Tumors at any place in the brain are likely to obstruct the flow of the cerebrospinal fluid. When this occurs the pressure builds up in the brain, producing the characteristic headache symptoms. In some manner this pressure is transmitted by way of the optic nerves and produces a swelling in the nerve heads known as "choked disks." In the early stages this swelling or choking of the disk causes no visual difficulty and is of importance only as an indication to the examiner of trouble in the brain. . . . The usual "stroke," when it affects the vision, blacks out a half of the patient's visual field. This occurs because the condition involves one side of the brain and, just as it may paralyze the opposite side of the body, it may likewise affect the opposite side of the patient's vision. This loss of vision is referred to as "homonymous hemianopsia"; that is, one half of each eye is blinded. . . . When a "stroke" results from basilar artery disease, the patient may be completely blind or so nearly blind that he has no useful vision. A number of the patients will have warning of impending trouble in that they experience transient blacking out of their vision along with other transient neurologic troubles.—T. P. Kearns, M.D., Diagnosis and Treatment of Neurologic Eye Disease, *The Sight-Saving Review*, Summer, 1956.

COUNCIL ON NATIONAL DEFENSE

Local Medical Disaster Preparedness

The disaster committee of the Alameda–Contra Costa County Medical Association of California prepared, with the assistance of the local civil defense offices, "Disaster Planning for Medical Services" and published it in April, 1956. The following report is based on the concepts of that local medical plan. It was prepared as a summary of their disaster planning with the cooperation of the Oakland office of Civil Defense and Disaster.

The Council on National Defense of the American Medical Association believes this report will be of interest to local medical societies and perhaps it may encourage them to prepare their own medical disaster plans, if they do not already have one.

Frank W. Barton, *Secretary.*

ORGANIZED MEDICINE AND CIVIL DISASTER

Wayne P. Chesbro, M.D., Berkeley, Calif.

The need for medical and health services disaster planning for the care of civilian populations became apparent during World War II when reports of the devastation wrought by explosive missiles in Britain and Germany were received. The magnitude of destruction of life and property was something never before envisioned. As was expected, civil disaster planning and services were developed to a high degree of efficiency in the countries affected by such destructive weapons. With the closing of World War II on the ominous note of the total destruction wrought by nuclear weapons, together with the growing conviction that geographical location was no longer a protection against nuclear warfare, the need for civil disaster planning, whether for "survival" in an all-out nuclear war or for the adequate medical care of casualties in a large-scale local disaster, was recognized by most state and county civil defense administrators.

Noting the meager personnel that carried on civil disaster planning for medical and health services in California and throughout the United States, and cognizant of the need for participation of organized medicine in such planning, the disaster committee of the Alameda–Contra Costa Medical Association began the initial study and planning for the activities of the medical and health services in order to offer to the local civil disaster departments the guidance, resources, and support of a local, organized medical association composed of a group of some 1,500 physicians serving an estimated population of one million in the two East Bay counties, a target area.

Chairman, Alameda–Contra Costa Medical Association Disaster Committee.

The association in committee discussion developed the concept that for efficient civil disaster planning, state medical associations down to the county level should assume direct responsibility for the plans of the medical and health services division. It is our firm conviction that, if physicians are to be called upon to serve in any disaster, their state and local medical organizations, with the concurrence of the state civil defense disaster offices, should designate the procedures they are to follow. It was also recognized that, in order to spark the interest of the medical group and to keep the activity alive, the planning must not be too detailed or involved and, most emphatically, should be geared first to the real potentialities of local disasters. For purposes of definite committee action, initial disaster planning was divided into three phases; in order of importance, hospital disaster planning, large-scale local disaster planning, and total disaster planning.

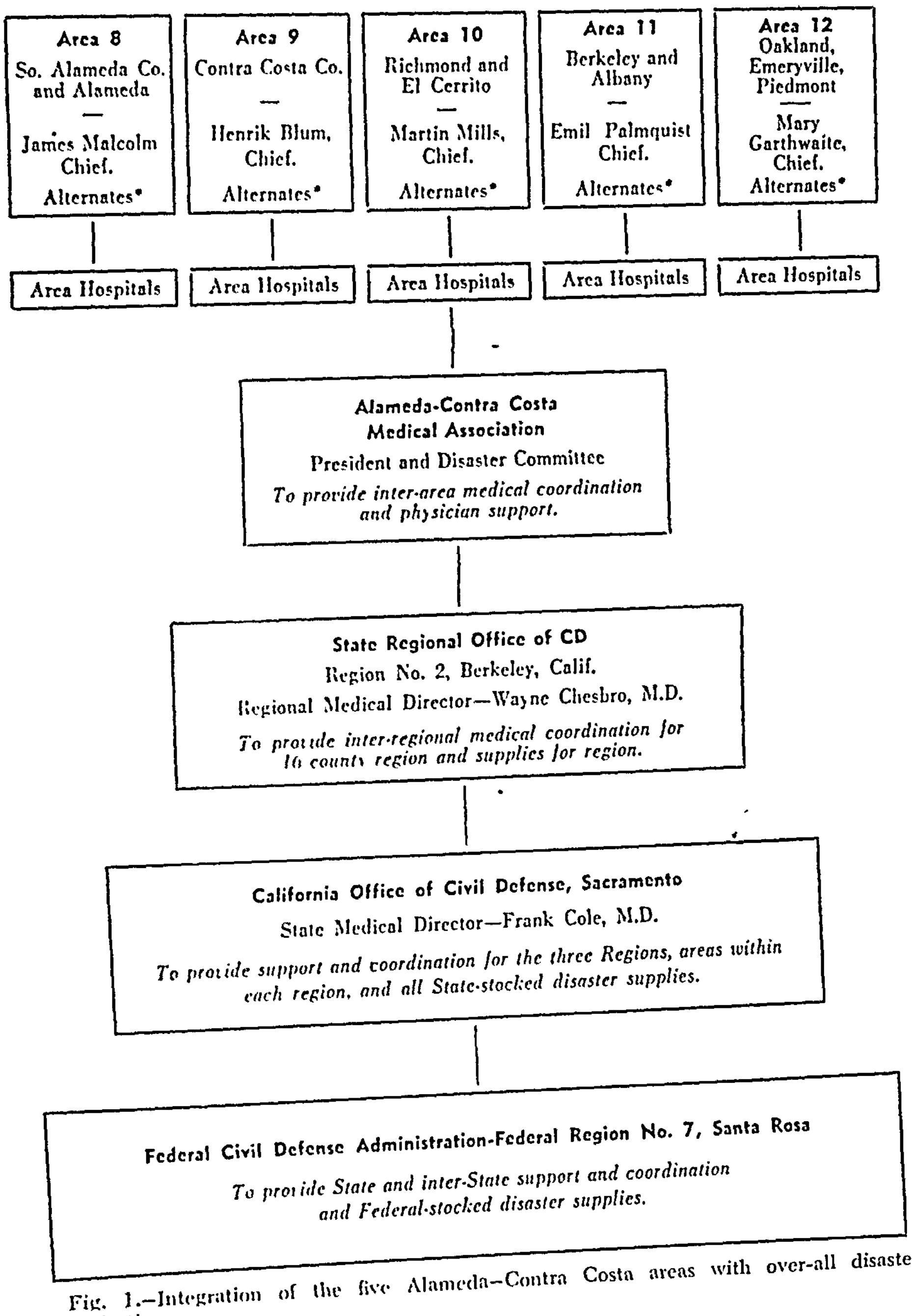
Area 8
So. Alameda Co. and Alameda
James Malcolm Chief.
Alternates*
Area 9
Contra Costa Co.
Henrik Blum, Chief.
Alternates*
Area 10
Richmond and El Cerrito
Martin Mills, Chief.
Alternates*
Area 11
Berkeley and Albany
Emil Palmquist Chief.
Alternates*
Area 12
Oakland, Emeryville, Piedmont
Mary Garthwaite, Chief.
Alternates*
Area Hospitals
Area Hospitals
Area Hospitals
Area Hospitals
Area Hospitals
Alameda-Contra Costa Medical Association
President and Disaster Committee
To provide inter-area medical coordination and physician support.
State Regional Office of CD
Region No. 2, Berkeley, Calif.
Regional Medical Director—Wayne Chesbro, M.D.
To provide inter-regional medical coordination for 16 county region and supplies for region.
California Office of Civil Defense, Sacramento
State Medical Director—Frank Cole, M.D.
To provide support and coordination for the three Regions, areas within each region, and all State-stocked disaster supplies.
Federal Civil Defense Administration-Federal Region No. 7, Santa Rosa
To provide State and inter-State support and coordination and Federal-stocked disaster supplies.

Fig. 1.—Integration of the five Alameda–Contra Costa areas with over-all disaster organization.

Hospital Disaster Planning

A medical association disaster committee should present to all hospital disaster committee chairmen a prototype hospital disaster plan. (Our association used the disaster plan of the Providence Hospital, Oakland, Calif.). A hospital disaster plan should encompass three divisions.

Division 1.—There should be hospital disaster planning for disaster within the hospital, such as that occurring from fire, explosion, earthquake, radiological contamination, or epidemic.

Division 2.—The hospital disaster plan should include planning for a large-scale local disaster occurring within the community or area in which the hospital is resident and in which the facilities of the hospital remain functional.

Division 3.—Hospital disaster planning should include a program for total disaster in which the hospital must undergo evacuation to and reconstitution of personnel and materials in a peripheral area and still function to its greatest capability in accepting the casualty load thrust upon its meager resources and surviving personnel.

Hospital disaster planning, at best, will proceed slowly, and committee members should be chosen for their patience and perseverance, for they will have much need for both. A copy of the Providence Hospital disaster plan is available to anyone interested in using it as a reference in developing workable plans for his own hospital.

Large-Scale Local Disaster Planning

For purposes of complete coverage of disaster within Alameda and Contra Costa counties, the two counties are divided into five operational areas. Reference to figure 1 will explain the jurisdictional areas as existent in the planning of the association. All areas have a chief of medical and health services with alternates in sufficient numbers to "cover" the duty at all times. In the event of a disaster within the area, the designated chief immediately becomes the medical officer in charge. He represents the president of the medical association at the disaster site. First-aid care, casualty evacuation to area hospitals, requests for additional medical and nursing personnel, mobile aid teams, and supplies all originate with the area chief of the medical and health services.

Reference to figure 2 shows the basic concept of the function of the area chief, medical and health services, in the disaster area. The function of the medical association disaster committee, at the association headquarters, will be to fill the requests of the area chief and to coordinate all other area facilities for mutual support. In the event of a large-scale local disaster involving more than one area, over-all authority should be directed from the medical association headquarters by the president or his designate, the chairman of the disaster committee. All physicians appointed within the areas as chiefs or alternates should be members of the medical association. In large-scale local disaster planning, there should be complete integration of the medical and health services plans with the existing civil disaster coordinators, Red Cross, and armed forces available to serve in disasters, the area hospitals, the physician assigned to disaster stations, the allied medical professions, and the local industry disaster planning.

Existing Civil Disaster Coordinators, Red Cross, and Armed Forces.—In order that all levels may function to mutual aid and support, orientation of command physicians (area chiefs, alternates, disaster committee members) should begin at the area level and extend from local civil disaster departments through regional jurisdictions to state headquarters. All concerned should be cognizant of existing civil disaster supplies and familiar with designated civil defense emergency hospitals and aid stations. Information should be available covering liaison facilities, established by mutual agreement, of the Red Cross and the armed forces of the immediate and adjacent areas and air transport service (especially helicopter) available in large-scale local disaster. Our association has, through the facilities of the U. S. Coast Guard, conducted an aerial survey of all the major hospitals of the two counties. U. S. Coast Guard helicopter service is now available in emergency cases authenticated by the association's disaster committee.

Area Hospitals.—The area chief of the medical and health services and his alternates should schedule regular meetings with their respective hospital administrators and disaster committee chairmen so that mutual planning will be kept current and well integrated. Hospital administrators should have available at all times a daily census of patients, with special reference to the numbers who can be moved or become ambulatory in order to permit rapid bed expansion in event of disaster. A census of the medical and technical personnel of the hospital on a 24-hour basis should be available. There should be provision for supplies necessary to continue operation of the hospital with an additional 75% increase in patient load for a 24-hour period.

Physician Assignments to Disaster Stations.—All assignments of physicians to disaster stations should be made by the disaster committee of the medical association. All hospitals should be asked to submit the names of the staff members who are to be considered as essential to the function of the hospital during an emergency. In the assignments of physicians, duplication of highly specialized skills should be avoided if possible. All physicians should be assigned to a hospital staff as a primary assignment for large-scale local disaster. Mobile medical teams and supplies should emigrate from the hospital to the scene of the disaster upon request of the area medical chief.

Allied Medical Professions.—A census should be made of the allied medical professions (nursing, dentistry, pharmacy, veterinary medicine, optometry, chiropody) and the technical services (laboratory and x-ray technicians, physiotherapists, dietitians) in each area. Assignments should be made from these groups to the area hospitals with the understanding that their function would be to serve as an auxiliary staff under the regular staff of the hospital in the event of a large-scale local disaster. Provision should be made for the indoctrination of this personnel, and their duties in the hospital or aid station should be delineated. Short courses should be given members of the dental and veterinary medical professions covering their roles as physicians' assistants. Definite hospital disaster assignments will maintain the interest of members of these allied medical professions in disaster planning.

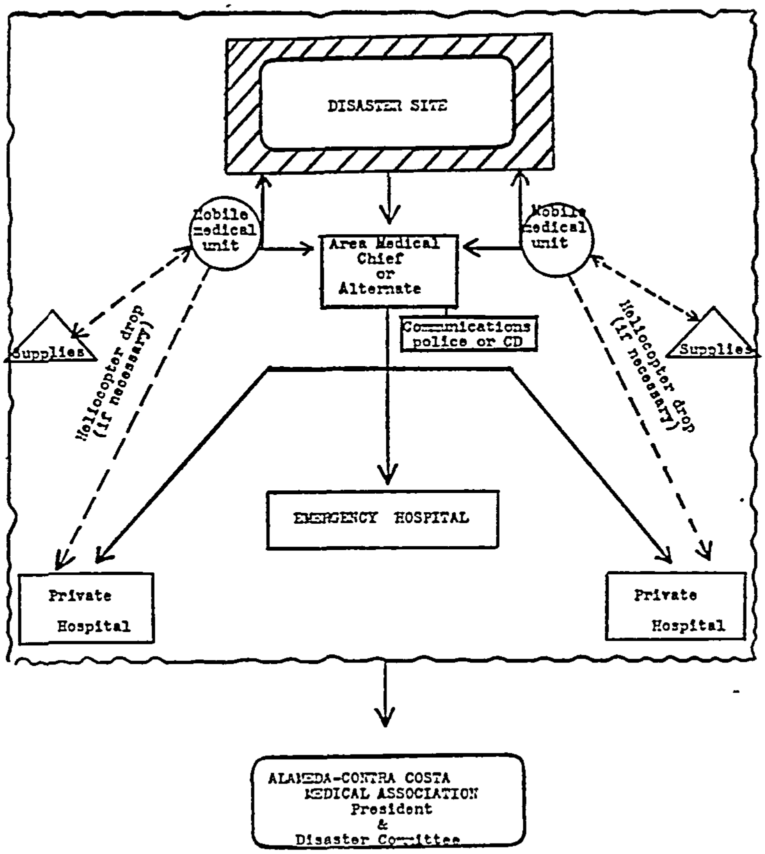
DISASTER SITE
Mobile medical unit
Mobile medical unit
Area Medical Chief or Alternate
Communications police or CD
Supplies
Supplies
Helicopter drop (if necessary)
Helicopter drop (if necessary)
EMERGENCY HOSPITAL
Private Hospital
Private Hospital
ALAMEDA-CONTRA COSTA MEDICAL ASSOCIATION President & Disaster Committee

Fig. 2.—Organization applicable to each of the five disaster areas of Alameda-Contra Costa counties in a local disaster. No medical personnel will move into a disaster area unless requested by that area's medical chief or alternate at the disaster site. The area medical chief or alternate is in full command of all medical services in the area in which the disaster occurs. Helicopter service for medical use may be ordered only by the area chief or alternate. Such an order must be transmitted directly to the chairman of the disaster committee at association headquarters. In event of disaster in Alameda or Contra Costa County, a mobile communications unit from the Oakland civil defense is immediately attached to the headquarters for direct communication with the medical chief or alternate on the disaster site.

Local Industry in Disaster Planning.—Industry should be represented in civil disaster planning both at area and association headquarters levels. Since, in many instances, major catastrophes have their origin

This program has category 1 (formal) approval by the American Academy of General Practice. A luncheon will be held at 12:30 p. m. and a cocktail party from 5-6 p. m. A special program, including a fashion show, has been arranged for wives.

PENNSYLVANIA

Meeting on Industrial Health.—The 21st annual meeting of the Industrial Hygiene Foundation will be held at the Mellon Institute, Pittsburgh, Nov. 14-15. The Medical Conference Wednesday morning will include papers on pulmonary physiology as related to industrial chest diseases, effective educational techniques in health counseling, and legal aspects of industrial medical practice. The Legal Conference the same morning will be concerned with the medical and legal aspects of health problems incident to the industrial use of atomic energy. Pneumonoconiosis and occupational carcinogens will be considered at the Chemical-Toxicological Conference. The Joint Technical Conference Wednesday afternoon will bring together all the groups for a panel discussion on "Health Problems Involved in the Manufacture, Sale, and Use of Toxic Materials." Panelists will include a representative of management, an industrial physician, a lawyer, an engineer, an industrial toxicologist, and an insurance executive. Joseph C. Hinsey, Ph.D., director of the New York Hospital-Cornell Medical Center, New York, will discuss future industrial medical problems at the Management Conference on Thursday. Other topics to be considered include the health problems involved in automation, the importance of epidemiology in determining whether a health problem actually exists, new channels of communication between management and technical personnel in matters of industrial health, management's views on industrial health problems, and systematic attention to health in operations research.

Philadelphia

Institute for Care of Cardiac Child.—An Institute for the Care of the Cardiac Child will be held at Children's Heart Hospital of Philadelphia, Nov. 7, to acquaint members of the medical, nursing, and social service professions with developments pertaining to young patients with heart disease. A tour of the spital will precede discussions on the recognition and treatment of congenital heart disease, the active stage of rheumatic fever, and rheumatic valvular disease. Afternoon sessions (2-4 p. m.) will consider other aspects of the subject. The luncheon speaker will be Dr. Hugh Montgomery, associate professor of medicine, University of Pennsylvania School of Medicine, and chief of the vascular section, University of Pennsylvania Hospital. The chairman of the institute is Dr. George D. Geckeler. The institute will be sponsored by the Children's Heart Hospital; Heart Association of Southeastern Pennsylvania; Department of Public Health, City of Philadelphia; School District of Philadelphia; Pennsylvania Heart Association; Department of Health, Commonwealth of Pennsylvania; Philadelphia County Medical Society; and the Hospital Council of Philadelphia.

TEXAS

Blackford Memorial Lecture.—The Grayson County Medical Society announces the first annual Blackford Memorial Lectureship on cancer at the Hotel Denison, Denison, Nov. 13, 1-5 p. m., in symposium form. Dr. Randolph L. Clark Jr., Houston, will monitor the program. The Blackford Memorial Fund, set up by Mrs. Clara Smith of Denison and Houston in honor of her father, who was a pioneer Denison banker, was established with the aim of having eminent authorities on cancer and cancer research as principal speakers and to keep the physicians of the area up-to-date on the latest progress in the field of cancer.

WISCONSIN

Pathologists Meeting.—The Wisconsin Society of Pathologists will hold its fall meeting at the Columbia Hospital Auditorium, 3321 N. Maryland Ave., Milwaukee, Nov. 12, 1:30 p. m. (sponsored by the Milwaukee County Chapter, American Cancer Society). The subject of the meeting will be "Collagen Diseases and Related Conditions." Dr. Milton G. Bohrod, pathologist and director of laboratories, Rochester General Hospital, Rochester, N. Y., will serve as moderator. Cocktails at 5:30 p. m. will precede dinner, 6:30 p. m., at the University Club, 924 E. Wells St., Milwaukee. Dr. John Z. Bowers, dean, University of Wisconsin Medical School, Madison, will speak on "Changing Concepts in the Teaching of the Basic Sciences."

GENERAL

Meeting of Teachers of Preventive Medicine.—The 13th annual meeting of the Association of Teachers of Preventive Medicine will be held in Atlantic City, N. J., Nov. 11. The first session at the Hotel Ambassador, 9 a. m., will include the following round tables:

Clinical Preventive Medicine, Glen R. Leymaster, Salt Lake City, chairman.
Epidemiology, John P. Fox, New Orleans, chairman.
Medical Care, Milton Terris, Buffalo, chairman.
Occupational Medicine, Jean S. Felton, Oklahoma City, chairman.
Public Health, Ray E. Trussell, New York, chairman.
Rehabilitation, Rodney R. Beard, San Francisco, chairman
Statistics, George F. Badger, Cleveland, chairman.

Dr. Duncan W. Clark, Brooklyn, N. Y., president, will preside over the second session at the Ritz Carlton Hotel, 2-5 p. m., when a panel will be presented on "Family Study and Care in Medical Education." Participants will include Dr. E. M. Holmes Jr., Richmond, Va.; Dr. John P. Hubbard, Philadelphia; Dr. John H. Kennell, Cleveland; J. Garth Johnson, Ph.D., Albany, N. Y.; Dr. George G. Reader, New York; and Dr. Robert E. Shank, St. Louis. At the dinner session, 6:30 p. m., Dr. Leona Baumgartner, New York, will speak on "Experiences in India" and Dr. John R. Paul, New Haven, Conn., will discuss "Experiences in the Soviet Union."

Electrical Techniques in Medicine and Biology.—The ninth annual Conference on Electrical Techniques in Medicine and Biology, sponsored by the American Institute of Electrical Engineers, the Institute of Radio Engineers, and the Instrument Society of America, will be held at the Governor Clinton Hotel, New York City, Nov. 7-9. A panel discussion on "Instrumentation for Cardiology," under the chairmanship of Dr. Lee B. Lusted, Bethesda, Md., will be presented Wednesday morning. Papers will include "A Cathode-Ray Cardiograph" and "High Voltage Condenser Discharge as a Means of Cardiac Resuscitation in Ventricular Fibrillation." The afternoon session will include a panel on "Methods and Standards for Measurement of Electron Beams," with Dr. John Laughlin, New York, as chairman. "The Philosophy Underlying Radiation Protection" will be presented that evening by Lauriston S. Taylor, Ph.D., chief, division of atomic and radiation physics of the National Bureau of Standards, Washington, D. C. A field trip to Brookhaven National Laboratory, Upton, Long Island, N. Y., is scheduled for Thursday. Friday morning a panel discussion will be concerned with "Design of Instruments for Research in Artificial Respiration." Papers to be delivered during the afternoon session on instrumentation in medicine and biology will include "Artificial Respiration Control" and "A New Type of Electroencephalograph Wave Analyser."

Annual Military Surgeons Convention.—The 63rd annual convention of the Association of Military Surgeons will be held at the Statler Hotel, Washington, D. C., Nov. 12-14. The theme of the meeting will be "The Expanding Horizons of Military Medicine." The presidential address will be delivered Monday, 9:15 a. m., by Rear Adm. Winfred P. Dana, M.C., U. S. Navy, assistant chief for aviation and operational medicine and research and medical military specialties, bureau of medicine and surgery, Department of the Navy, Washington, D. C. Detlev W. Bronk, Ph.D., president, National Academy of Sciences, Washington, D. C., will be the guest speaker at the morning session. An international luncheon will be held Tuesday, 1:30 p. m.; Adm. Arthur W. Radford, U. S. Navy, chairman, Joint Chiefs of Staff, Washington, D. C., will be the guest speaker. Meeting on Tuesday will be the dental, veterinary, sanitary engineering, and medical specialist sections. The latter section, meeting at 3 p. m., will include discussion of "Medical Research Today" by Dr. Stuart M. Sessoms, assistant director, Clinical Center, National Institutes of Health, Bethesda, Md., and a panel on "Medical Research in Total Research Hospital Setting and Its Impact on the Nutrition, Physical Therapy, and Occupational Therapy Services," with Dr. John L. Fahey, general medicine branch, National Cancer Institute, Bethesda, Md., as a participant. The sustaining membership and nursing sections will meet on Wednesday.

Meeting of Inhalation Therapists.—The annual meeting and lecture series of the American Association of Inhalation Therapists will be held at the Park Sheraton Hotel, New York, Nov. 12-16. Physicians will make the following presentations:

Pressure Breathing, Peter A. Theodos, Philadelphia.
Inhalation Therapy in Controlling Diseases of the Chest, Edwin R. Levine, Chicago.
Resuscitation: Including the Cardiac Arrest Problem, Virginia Apgar, New York.
Physiologic Basis of Inhalation Therapy, Alvan L. Barach, New York.
Aerosol Therapy, Hylan A. Bickerman, New York.
Bronchial Drainage: Including Exsufflation, Gustav J. Beck, New York.
Inhalation Therapy in Acute Obstructive Diseases, Albert H. Andrews Jr., Chicago.
Bronchiolitis and Pneumonia in Infants and Children, Milton I. Levine, New York.
Inhalation Therapy in the Treatment of Smoke, Gas, and Fume Poisoning, Maurice S. Segal, Boston.
Oxygen Therapy and Prevention of Retrolental Fibroplasia, Charles U. Letourneau, Chicago.
Qualifications for Inhalation Therapists, Edwin Emma, New York.
Tent Therapy, Alvis E. Greer, Houston, Texas.
Organizing an Inhalation Therapy Department, Gordon M. Wyant, Saskatoon, Saskatchewan, Canada.

Field trips have been arranged to the headquarters of the emergency service division of the New York City Police Department, Tuesday, 7:30 p. m., and to the Presbyterian Medical Center, Wednesday, 7:30 p. m. At 12:30 p. m. Friday, Drs. Greer, Wyant, and Vincent J. Collins, New York, will participate in a panel entitled "Selling the Hospital Administrator on an Inhalation Therapy Department."

Chest Physicians Meeting.—The Potomac and Southern chapters of the American College of Chest Physicians will hold a joint meeting at the Shoreham Hotel, Washington, D. C., Nov. 11-12. Single-author presentations will include:

Pulmonary and Metabolic Aspects of Cystic Fibrosis (Mucoviscidosis), Paul A. di Sant'Agnese, New York.
Current Status of the Pneumonias, Robert C. Austrian, New York.
Pathogenesis and Treatment of Peripheral Vascular Collapse Associated with Fulminant Diffuse Pulmonary Infiltrations, Donald W. Seldin, Dallas, Texas.
Application of Hypothermia in the Correction of Cardiovascular Lesions, Major Edward J. Jahnke Jr., Washington, D. C.
Severe Crushing Injuries of the Chest: A New Method of Treatment, Edward E. Avery, Chicago.
Features and Significance of Hypertrophic Osteoarthropathy, James F. Hammarsten, Oklahoma City.
Ten Years of Tuberculosis Surgery, J. Maxwell Chamberlain, New York.
Controversial Aspects of the Surgery of Tuberculosis, James D. Murphy, Baltimore.

At 12 noon Sunday, Dr. William F. Miller, Dallas, Texas, will serve as moderator for a panel entitled "Physiologic Therapy of Bronchopulmonary Disease," for which the participants will be Drs. Alvan L. Barach, New York, and Maurice S. Segal, Boston. Drs. Otto C. Brantigan and Ross L. McLean, Baltimore, and Sol Katz, Washington, D. C., will participate in an x-ray conference at 4 p. m., moderated by Dr. Charles N. Davidson, Baltimore. A cocktail party at 6 p. m. (courtesy of the Potomac chapter) will precede the banquet ($6.50, including gratuity and tax). The third Paul Turner Memorial Lecture (sponsored by the Southern chapter) will be presented at 8:15 p. m. by Dr. O. Theron Clagett, Rochester, Minn., who will discuss "Carcinoma of the Lung."

Southern Medical Association.—The golden anniversary meeting of the Southern Medical Association will be held at the Sheraton-Park Hotel, Washington, D. C., Nov. 12-15 (30 hours credit, American Academy of General Practice). The program Monday will be opened by Dr. Ralph M. Caulk, president, Medical Society of the District of Columbia, and will include 15 presentations by Washington physicians, in addition to a panel discussion entitled "Preoperative Evaluation and Choice of Anesthesia in Surgical Patients with Reduction of Circulatory Reserve," Dr. William E. Bageant, Washington, D. C., moderator. The first general session at the Mayflower Hotel, Monday, 8 p. m., will include the presidential address by Dr. W. Raymond McKenzie, Baltimore, and presentation of the Certificate of Meritorious Service to Dr. Margaret M. Nicholson, Washington, D. C., and the John Benjamin Nichols award to Mr. Joseph H. Himes, Washington, D. C. At the second general session Wednesday, 8 p. m., Dr. David B. Allman, Atlantic City, N. J., President-Elect, American Medical Association, will deliver an address entitled "Who Will Carry the Torch?" A Geriatrics Symposium will be held Thursday, 9 a. m. at the Sheraton, with Dr. Milford O. Rouse, Dallas, Texas, as moderator. More than 300 papers will be presented during the assembly, which includes 20 section meetings. Twenty motion pictures will be shown Tuesday, Wednesday, and Thursday. The Southern Flying Physicians will hold a luncheon and scientific program Tuesday at the Mayflower Hotel. The preliminary program lists 19 medical schools that will hold alumni and fraternity reunions during the meeting. The annual golf tournament will be held at the Kenwood Golf and Country Club, Bethesda, Md., Monday.

Association of American Medical Colleges.—The 67th annual meeting of the Association of American Medical Colleges will be held at the Broadmoor Hotel, Colorado Springs, Colo., Nov. 12-14. Preconference meetings of the standing committees will be held on Sunday, Nov. 11. Copies of the annual reports of these committees will be presented to each person as he registers, and open hearings on them will be held at 4:00 p. m. on Monday. Dr. Robert A. Moore, president of the association, will present his address on Monday, 9:30 a. m. At the annual dinner Monday evening, the Borden award will be presented and Adolph W. Schmidt, president of the A. W. Mellon Educational and Charitable Trust, will present an address. On Monday and Tuesday afternoons, 2:00 p. m., the general subject for discussion will be "Experiments in Medical Education," for which a number of speakers have been assigned special topics. On Wednesday, 9:00 a. m., Drs. John Z. Bowers and Robert C. Parkin, Madison, Wis., will discuss "A 'Twenty-Eight Year' Experiment in Preceptorial Medical Education"; Horace A. Page, Ph.D., Madison, Wis., "Description of a Study Designed to Evaluate Preceptorial Experience and Its Relation to the Plans, Skills and Attitudes of Senior Medical Students"; Drs. Henry J. Bakst and William Malamud, Boston, "Combined Teaching in Human Ecology"; Dr. Eugene A. Hargrove, Chapel Hill, N. C., "An Introduction to Clinical Medicine in the First Year"; and Granger Westberg, Chicago, "Religious Aspects of Medical Teaching." Some 15 papers will be read by title. A program of activities for the ladies has been arranged. For details of short tours in the mountains and elsewhere consult with Miss Allyn at the registration desk.

Gerontological Society Meeting.—The ninth annual scientific meeting of the Gerontological Society will be held at the Hotel Hamilton, Chicago, Nov. 8-10 under the presidency of Dr. William B. Kountz, St. Louis. The general session Thursday, under the chairmanship of Dr. Emmet B. Bay, Chicago, will consist of a panel on Progress in Gerontology and will include presentation of "Progress in Social Work and Administration" by Mrs. Elizabeth Breckinridge, Chicago; "Progress in the Biological Sciences" by Dr. George E. Wakerlin, Chicago; and "Progress in the Psychological and Social Sciences" by Ward C. Halstead, Ph.D., Chicago. The sections on biological sciences, clinical medicine, psychological and social sciences, and social work and administration will hold simultaneous meetings, Thursday, 2-4:30 p. m.; Friday and Saturday, 9:30-12 noon. The section on clinical medicine will present a clinic at Passavent Memorial Hospital, Friday, and the meeting Saturday will include a symposium moderated by Dr. Thomas H. McGavack of New York. The Friday session of the section on psychological and social sciences will consist of a symposium entitled "Assessment of Mental Health in the Elderly," under the chairmanship of Dr. Ewald Busse, Durham, N. C. The Thursday meeting of the section on social work and administration will consist of a panel on "Senile Patients and Their Care," and the Friday session will include a panel on "Adult Boarding Homes and Their Place in Community Resources for Older People." "Planning Education and Recreation Programs for Older People" will be the title of the social work section panel on Saturday. The evening session Thursday, 8 p. m., includes an illustrated lecture "Aging in the Atomic Age." The general session Friday, 2-5 p. m., will consist of a symposium on "Education for Maturity," moderated by Dr. Edward J. Stieglitz, Washington, D. C. Cocktails at 6 p. m. will

DEATHS

Davidoff, Eugene ⊕ Schenectady, N. Y.; born in New York City May 11, 1901; State University of Iowa College of Medicine, Iowa City, Iowa, 1927; associate professor of psychiatry at Albany (N. Y.) Medical College; at one time on the faculty of the Syracuse (N. Y.) University College of Medicine, specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association and the American Psychopathological Association; associated briefly with Willard (N. Y.) State Hospital before becoming clinical director at Craig Colony, Sonyea, in 1943; during World War II joined the armed forces as a lieutenant colonel and finally served in this capacity as chief neuropsychiatrist for the Veterans Administration at Watervliet; at one time in charge of the mental hygiene clinic at Syracuse (N. Y.) Psychopathic Hospital; child psychiatrist of Ellis Hospital; joint author with Elinor S. Noetzel of a book entitled "The Child Guidance Approach to Juvenile Delinquency"; died while vacationing at Cape Cod, Mass., July 23, aged 55, of a heart attack.

Falconer, Ernest Henry ⊕ San Francisco; born in Pardeeville, Wis., May 19, 1883; McGill University Faculty of Medicine, Montreal, Quebec, Canada, 1911; clinical professor of medicine emeritus at the University of California School of Medicine, where in 1921 he became chief of the blood clinic, which he had established; fellow and long governor for Northern California of the American College of Physicians, appointed to its board of regents in 1947 and made first vice-president in 1950; during World War I was with Base Hospital 30, the University of California Unit, in France; specialist certified by the American Board of Internal Medicine; consultant in hematology, Franklin Hospital and Children's Hospital; visiting physician at the University of California Hospital; on May 27, 1953, the McGill University in Montreal, Quebec, Canada, conferred on him an honorary LL.D degree; died in Los Gatos, Aug. 11, aged 73.

Spitz, Sophie ⊕ New York City; born in Nashville, Tenn., Feb. 4, 1910; Vanderbilt University School of Medicine, Nashville, Tenn., 1932; specialist certified by the American Board of Pathology; member of the American Association of Pathologists and Bacteriologists and the American Society of Clinical Pathologists, assistant professor of pathology at the Sloan-Kettering division of Cornell University Medical College; formerly assistant medical examiner of New York City; during World War II was with the Army Institute of Pathology, now the Armed Forces Institute of Pathology; joint author of "Pathology of Tropical Diseases", director of the pathology department, New York Infirmary for Women and Children; assistant attending pathologist at Memorial Center for Cancer and Allied Diseases, where she died Aug. 10, aged 46, of recurrent carcinoma of the colon.

Harney, Charles Harrison, Sewickley, Pa.; born in Lexington, Ky., July 11, 1900; Columbia University College of Physicians and Surgeons, New York City, 1929; member of the Tennessee State Medical Association; certified by the National Board of Medical Examiners; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; veteran of World Wars I and II; retired from the Veterans Administration Sept. 30, 1953; formerly chief of the surgical service of the Veterans Administration Hospital in Mountain Home, Tenn., served on the staffs of the Bryn Mawr (Pa.) Hospital and the Pennsylvania and Jefferson Medical College hospitals in Philadelphia; died July 6, aged 55, of coronary thrombosis.

Rabil, Pierre Jamil, Washington, D. C.; born Oct. 25, 1912, University of Montreal Faculty of Medicine, Montreal, Quebec, Canada, 1938; served on the faculty of his alma mater and McGill University in Montreal, Quebec, Canada, where he was on the staff of the Hopital Ste. Jeanne d'Arc; assistant professor of surgery at Georgetown University School of Medicine; a lieutenant colonel in World War II, served with the Army in the European Theater and was awarded the Bronze Star, the Purple Heart, and the French Legion of Honor and Croix de Guerre; on the staff of the Georgetown University Hospital, where he died July 23, aged 43.

Sharlit, Herman, New York City; born in New York City May 2, 1892; Cornell University Medical College, New York City, 1917; associate professor of clinical dermatology and syphilology at the New York Post-Graduate Medical School; formerly on the faculty of University and Bellevue Hospital Medical College; specialist certified by the American Board of Dermatology and Syphilology; member of the Medical Society of the State of New York, American Dermatological Association, and the American Academy of Dermatology and Syphilology; died while vacationing in Atlantic City, N. J., July 12, aged 64, of cerebral thrombosis.

Molloy, James Patrick, Houston, Texas; born in Chicago in 1895; Johns Hopkins University School of Medicine, Baltimore, 1921; clinical associate professor of psychiatry at Baylor University College of Medicine; at one time on the faculty of Loyola University School of Medicine in Chicago, where he was once clinical director of the Institute of Juvenile Research; fellow of the American Psychiatric Association; on the staffs of St. Joseph's, Methodist, and Montrose hospitals; member of the board of trustees of Hedgecroft Hospital and Clinic; died July 21, aged 61, of cerebral thrombosis.

Shuman, John William, Sr., Santa Monica, Calif.; University of Pittsburgh School of Medicine, Pittsburgh, 1910; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; an associate member of the American Medical Association; veteran of World Wars I and II; served as consultant in medicine, Presbyterian Hospital–Olmsted Memorial in Los Angeles; senior attending physician, emeritus, Los Angeles County Hospital; formerly on the staff of the Veterans Administration Center in West Los Angeles; died Aug. 4, aged 71, of carcinoma of the bladder.

Akin, William Edwin, Jr., Paintsville, Ky.; University of Louisville School of Medicine, Louisville, 1931; fellow of the American College of Surgeons; veteran of World War II; past-president of the Johnson County Medical Society; an associate member of the American Medical Association; died in the Veterans Administration Hospital, Louisville, Aug. 2, aged 54, of cerebral thrombosis and femoral artery occlusion.

Ayers, Thomas Fred ⊕ San Francisco; University of California School of Medicine, San Francisco, 1920; served an internship and residency at Santa Clara County Hospital in San Jose; died June 21, aged 69, of hypertension and arteriosclerotic heart disease.

Baker, William Pope, Atlanta, Ga.; Emory University School of Medicine, Emory University, 1920; an associate member of the American Medical Association; fellow of the American College of Physicians; died July 11, aged 62.

Barber, Ira Zelna, Princeton, Ky.; University of Louisville Medical Department, Louisville, 1905; served as city and county physician; died June 17, aged 78.

Barshak, Max ⊕ New York City; University and Bellevue Hospital Medical College, New York City, 1915; died aboard the Grace Liner Santa Clara, Aug. 6, aged 67, en route to Venezuela.

Bell, Firman Merrill, Grant, Neb.; Central Medical College of St. Joseph, Mo., 1904; an associate member of the American Medical Association; for many years county physician; served as president of the Garden-Keith-Perkins Counties Medical Society; on the staff of the Perkins County Community Hospital; died Aug. 4, aged 83, of carcinoma of the colon.

Bourne, Ulysses Grant, Sr., Frederick, Md.; Leonard Medical School, Raleigh, N. C., 1902; an associate member of the American Medical Association; died in the Frederick Memorial Hospital July 15, aged 82, of cerebral hemorrhage.

Breen, Adrian Louis, Farley, Iowa; L.R.C.P., London, and M.R.C.S., of England, 1894; served in France during World War I; for many years a member and for one year president of the school board; formerly assistant superintendent of the Independence (Iowa) State Hospital; died in the Xavier Hospital, Dubuque, July 16, aged 83, of cancer.

⊕ Indicates Member of the American Medical Association.

Breslin, William Aloysius ⊕ Shenandoah, Pa.; Jefferson Medical College of Philadelphia, 1916; veteran of World War I; served in the regular U. S. Navy; past-president of the Shenandoah Medical Society; died July 18, aged 63, of cor pulmonale and congestive heart disease.

Bromund, Emile Herman, Oberlin, Ohio; Jenner Medical College, Chicago, 1905; died May 12, aged 84, of nephrosclerosis and arteriosclerosis.

Campbell, Isaac Augustus, Los Angeles; Kansas City (Mo.) Medical College, 1905; at one time health and quarantine officer for the United States at the Mexican port of Vera Cruz; died in the California Lutheran Hospital, July 30, aged 77, of carcinoma of the stomach.

Carmichael, Marvin Monroe, Osage, Okla.; Mississippi Medical College, Meridian, 1911; at one time associated with the Indian Service; died July 21, aged 70.

Coffield, Franklin Carver, Salem, Ky.; Hospital College of Medicine, Louisville, 1904; member of the Kentucky State Medical Association; died in Paducah July 10, aged 80.

Cook, Thomas Wood, Allentown, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1912; an associate member of the American Medical Association; fellow of the American College of Surgeons; on the staff of the Graduate Hospital of the University of Pennsylvania, Philadelphia, and the Sacred Heart Hospital; died July 29, aged 70, of coronary occlusion.

Cowie, Helen Jean, Redwood City, Calif.; Woman's Medical College of Pennsylvania, Philadelphia, 1906; died July 15, aged 81, of arteriosclerosis.

Cummings, Arthur Hibbard, Mesa, Ariz.; University of Buffalo School of Medicine, Buffalo, 1922; member of the Medical Society of the State of New York; an associate member of the American Medical Association; for many years district health officer for the New York State Health Department; during World War II served with the U. S. Public Health Service; served as director of the city health department of Portmouth, Va.; died Aug. 22, aged 60.

Davis, Elijah Gillam, Champaign, Ill.; St. Louis College of Physicians and Surgeons, 1891; died in the Carle Memorial Hospital, Urbana, July 26, aged 87, of cerebral vascular accident.

Davis, Robert I. ⊕ Birch Tree, Mo.; University of Louisville (Ky.) Medical Department, 1909; died July 2, aged 85.

DeLay, Eli Milton, Sulphur, Okla.; Bennett Medical College, Chicago, 1915; veteran of World War I; died July 21, aged 62, of carcinoma of the stomach with metastases.

Disbrow, G. Ward ⊕ Owensboro, Ky.; University of Maryland School of Medicine, Baltimore, 1913; specialist certified by the American Board of Radiology; member of the American College of Radiology; past-president and secretary of the Daviess County Medical Society; veteran of World War I; served on the Medical Milk Commission in New Jersey, and was a member of the Summit, N. J., Board of Health; on the staff of the Owensboro-Daviess County Hospital, where he died July 22, aged 66.

Druckerman, Leonard James ⊕ New York City; Cornell University Medical College, New York City, 1931; specialist certified by the American Board of Surgery; associate attending surgeon at the Mount Sinai Hospital; fellow of the American College of Surgeons; died July 30, aged 49, of acute coronary thrombosis.

Eastman, Henry Allen, Jamestown, N. Y.; University of Buffalo School of Medicine, Buffalo, 1892; died Aug. 26, aged 88.

Enniss, Joseph, Waynesboro, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1899; an associate member of the American Medical Association; died June 28, aged 81, of hypertension and cerebral hemorrhage.

Felker, Gertrude ⊕ Dayton, Ohio; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1901; named "the 1954 Woman of the Year" by the Dayton Business and Professional Women's Club; said to be the first woman physician to practice in Dayton; a determined pioneer in promoting the public health of her community, starting with a safe milk campaign long before the days of pasteurization; died July 22, aged 83, of coronary occlusion.

Finkelberg, Ivan Lewis ⊕ San Bernardino, Calif.; Loyola University School of Medicine, Chicago, 1916; member of the American Urological Association; died July 18, aged 65.

Fitzpatrick, Joseph W., Anchorage, Ky.; Hospital College of Medicine, Louisville, 1900; died July 25, aged 81.

Fox, Norman Albright ⊕ Greensboro, N. C.; University of Pennsylvania School of Medicine, Philadelphia, 1924; veteran of World Wars I and II; on the staffs of the Moses H. Cone Memorial Hospital, Wesley Long Hospital, and the Piedmont Memorial Hospital; died in the Wesley Long Hospital July 17, aged 56, of coronary thrombosis.

François, Silvain Joseph Alexander ⊕ New Glarus, Wis.; Marquette University School of Medicine, Milwaukee, 1916; on the staff of St. Clare Hospital in Monroe; died July 23, aged 65, of coronary thrombosis.

Giffen, John R. ⊕ Bangor, Mich.; Willamette University Medical Department, Salem, Ore., 1894; for many years served on the school board; died in South Haven July 24, aged 85.

Greenberg, Morris ⊕ Forest Hills, N. Y.; New York Homeopathic Medical College and Flower Hospital, New York City, 1924; served on the faculty of his alma mater; member of the New York Academy of Sciences; formerly on the staffs of the Queens General Hospital and the Triboro Hospital of Queens Hospital Center in Jamaica; died in the Oneida (N. Y.) City Hospital Aug. 3, aged 67, of acute cerebral hemorrhage.

Hale, Douglas McCardell, Coldspring, Texas; Tulane University School of Medicine, New Orleans, 1926; member of the State Medical Association of Texas; died July 18, aged 54, of coronary occlusion.

Harvey, James Rufus ⊕ Footville, Wis.; Milwaukee Medical College, Milwaukee, 1910; member of the American Academy of General Practice; past-president of the Rock County Medical Society; veteran of World War I; on the staff of the Mercy Hospital in Janesville; a director and president of the Footville State Bank; died in Janesville July 19, aged 74, of chronic lymphatic leukemia.

Hintze, Anne Augusta, Reading, Mass.; Woman's Medical College of Pennsylvania, Philadelphia, 1903; died April 8, aged 92, of coronary thrombosis and arteriosclerosis.

Hollingsworth, Albert A. ⊕ Indianapolis; Medical College of Indiana, Indianapolis, 1905; on the staffs of St. Vincent's and Methodist hospitals; died July 22, aged 76, of cancer.

Holt, Russell Devereaux ⊕ Staunton, Va.; Medical College of Virginia, Richmond, 1899; for many years associated with the Indian Service; died July 26, aged 86, probably of ventricular fibrillation and arteriosclerotic cardiovascular disease.

Hoshino, Mitsuharu ⊕ Honolulu, Hawaii; University of Texas School of Medicine, Galveston, 1920; president of the staff of the Kuakini Hospital, where he was honorary life member; a life member of Queen's Hospital; died in St. Francis Hospital May 29, aged 59, of cerebral hemorrhage.

Kapp, Henry ⊕ Haverhill, Mass; Tufts College Medical School, Boston, 1911; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; veteran of World War I; chairman of the board of trustees of the Haverhill Municipal Hospitals (Hale); on the staff of the Haverhill Municipal Hospitals; died July 24, aged 66, of carcinoma of the lung.

Kelley, Edward Joseph, Watertown, Mass.; Tufts College Medical School, Boston, 1913; served on the teaching staff of his alma mater; for six years on the board of health, two of them as chairman; for many years associate medical examiner for the seventh Middlesex district and school physician; served on the staffs of the Mount Auburn Hospital in Cambridge and the Waltham (Mass.) Hospital; died July 24, aged 67, of carcinoma of the throat and pneumonia.

Kirkup, Norman Nelson, Detroit; University of Toronto Faculty of Medicine, Toronto, Ontario, Canada, 1919; died July 17, aged 62.

Krombein, Walter Henry ⊕ Buffalo; University of Buffalo School of Medicine, Buffalo, 1924; assistant professor of medicine at his alma mater; specialist certified by the American Board of Internal

Medicine; fellow of the American College of Physicians; consultant in internal medicine to the U. S. Public Health Service; on the staffs of St. Francis Hospital and the Buffalo General Hospital, where he died July 24, aged 55.

Langhoff, Arthur Harry ⊕ Mankato, Minn.; University of Minnesota Medical School, Minneapolis, 1922; died June 20, aged 66.

Liles, Nelson Pickett, Bastrop, La.; Medical College of South Carolina, Charleston, 1911; for many years director of the Morehouse health unit; died July 24, aged 71, of Parkinson's disease.

Lowry, James Cage, Dallas, Texas; Louisiana State University School of Medicine, New Orleans, 1955; intern, Methodist Hospital; died in Mineral Wells June 16, aged 26, in a private aircraft accident.

Mangan, Edward McDonnell, Forest Hills, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1947; member of the American Trudeau Society; served on the staffs of the Triboro Hospital of Queens Hospital Center and the Mary Immaculate Hospital in Jamaica; died April 1, aged 32.

Martin, James William ⊕ Omaha; Creighton University School of Medicine, Omaha, 1921; professor of orthopedic surgery at his alma mater; specialist certified by the American Board of Orthopaedic Surgery; member of the Clinical Orthopaedic Society and the American Academy of Orthopaedic Surgeons; fellow of the American College of Surgeons; for many years on the staff of Creighton Memorial St. Joseph's Hospital; died in Rochester. Minn., July 20, aged 60, of pulmonary edema and coronary sclerosis.

Meredith, Harold Hamilton ⊕ Oakland, Calif.; Gross Medical College, Denver, 1899; on the staff of Peralta Hospital; died Aug. 6, aged 77, of coronary sclerosis.

Metcalfe, Brice Fields, Greenville, Ohio; Medical College of Ohio, Cincinnati, 1899; served as secretary of the Darke County Medical Society; associated with the Wayne Hospital; died Aug. 3, aged 82, of arteriosclerosis.

Minor, Samuel West, Hinton, Okla.; University of Tennessee Medical Department, Nashville, 1905; an associate member of [illegible]e American Medical Association; died July 4, aged 84, of purulent urinary cystitis.

Morrill, Walter LeRoy, Sterling, Neb.; Omaha Medical College. Omaha, 1895; served on the staff of St. Elizabeth Hospital in Lincoln; died in Lincoln July 27, aged 83, of arteriosclerosis.

Moss, Daniel B., Palmyra, Mo.; Missouri Medical College, St. Louis, 1896; retired Sept. 15, 1938, as chief medical officer of the Chicago, Burlington and Quincy Railroad; at one time secretary of the American Association of Railway Surgeons; died July 21, aged 84.

Mowry, Harry Dale ⊕ Ambridge, Pa.; Jefferson Medical College of Philadelphia, 1926; on the staff of the Sewickley Valley Hospital in Sewickley; died in Monroeville July 24, aged 54, of acute hemorrhagic pancreatitis and coronary artery insufficiency.

Nevarez Izurieta, Miguel Angel ⊕ McAllen, Texas; Universidad Nacional Facultad de Medicina, Mexico, D. F., 1928; died near Armstrong April 15, aged 51, in an automobile accident.

Resmer, Norbert Joseph, Pittsburgh; Western Pennsylvania Medical College, Pittsburgh, 1902; an associate member of the American Medical Association; served as health examiner for the Mount Oliver (Pa.) School District; member of the staff of St. Joseph's Hospital and Dispensary, where he died July 7, aged 77, of carcinoma of the stomach.

Roberts, Buford Benjamin ⊕ Hawthorne, Calif.; University of Oklahoma School of Medicine, Oklahoma City, 1927; member of the American Academy of General Practice; member, and past vice-president and secretary of the staff of the Hawthorne Community Hospital; on the staff of the Centinela Valley Community Hospital in Inglewood; died in Inglewood July 9, aged 56, of arteriosclerotic heart disease.

Robinson, Fred Lawrence ⊕ Dearborn, ity of
Michigan Medical School, Ann Arbor, 19. World
War I; on the staffs of the Mount Carme l in
Detroit and the Oakwood Hospital; died Ju of
coronary disease.

Robinson, Marion Marshall, Richmond, Ky.; University of Louisville School of Medicine, 1914; served a term on the state legislature; on the staff of the Pattie A. Clay Infirmary; died July 1, aged 71, of coronary occlusion.

Rogers, William J., Connerville, Okla. (licensed in Oklahoma under the Act of 1908); died June 24, aged 84.

Ryan, Terence Cullen ⊛ Springfield, Mass.; Harvard Medical School, Boston, 1924; certified by the National Board of Medical Examiners; on the staffs of the Wesson Memorial Hospital and the Mercy Hospital, where he died July 6, aged 58, of coronary sclerosis with occlusion.

Ryan, Thomas Addis, Albany, N. Y.; Albany (N. Y.) Medical College, 1893; an associate member of the American Medical Association; served on the staff of St. Peter's Hospital; died Aug. 1, aged 91, of coronary thrombosis.

Salvatore, Victor L., New York City; Fordham University School of Medicine, New York City, 1916; died July 9, aged 66, of adenocarcinoma of the bladder.

Sanborn, Warren Bigelow, Harmony, R. I.; Atlantic Medical College, Baltimore, 1909; veteran of World War I; served as superintendent of the Augusta (Maine) General Hospital and the State Home and School at Providence; died June 16, aged 78.

Sarnelli, Ciriaco A., New York City; Regia Università di Napoli Facoltà di Medicina e Chirurgia, Italy, 1923; member of the Medical Society of the State of New York; died in the Neurological Institute July 18, aged 58, of bronchogenic carcinoma with metastases to the brain.

Schuldt, Theodore Scott, Pierceton, Ind.; University of Louisville (Ky.) School of Medicine, 1917; member of the Indiana State Medical Association; served as county health officer; veteran of World War I; died in Columbia City July 1, aged 67, of cerebral hemorrhage and arteriosclerotic heart disease.

Seal, Herman ⊕ Captain, U. S. Navy, retired, Encino, Calif.; Tulane University School of Medicine, New Orleans, 1922; retired from the regular Navy January, 1946; member of the American Academy of General Practice; on the staff of the Valley Hospital in Van Nuys; died July 2, aged 56.

Seiler, Elizabeth S., Milwaukee; Ludwig-Maximilians-Universität Medizinische Fakultät, München, Bavaria, Germany, 1921; died July 16, aged 61.

Shearer, Harry Arthur ⊕ Beloit, Wis.; Marquette University School of Medicine, Milwaukee, 1919; member of the American Academy of Ophthalmology and Otolaryngology; specialist certified by the American Board of Otolaryngology; veteran of World War I; served on the staff of the Beloit Municipal Hospital; died in the University Hospital, Madison, July 27, aged 62, of pneumonia and diverticulitis.

Sherk, Joseph Huber ⊕ Midland, Mich.; Detroit College of Medicine, 1907; served as member and president of the school board; for many years on the Midland City Planning Commission; died June 8, aged 73, of coronary occlusion and cerebral thrombosis.

Sibley, Harry Alonzo ⊕ Pontiac, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1907; past-president of the Oakland County Medical Society; served on the board of education and as school physician; on the staffs of the Pontiac General and St. Joseph Mercy hospitals; died July 10, aged 74, of cerebral hemorrhage.

Simmons, Richard John ⊕ Elizabeth, N. J.; St. Louis University School of Medicine, St. Louis, 1942; veteran of World War II; died in the Veterans Administration Hospital, Albany, N. Y., July 18, aged 42.

Simpson, Charles J., Westminster, Texas; University of Louisville (Ky.) Medical Department, 1892; died in Sherman June 3, aged 86.

Sisson, Mabel Cornelia, Bayside, N. Y.; Boston University School of Medicine, Boston, 1899; died July 26, aged 82, of arteriosclerotic heart disease and cerebral thrombosis.

Si **Donnie,** Dade City, Fla.; Kentucky School of
M ville, Ky., 1898; an associate member of the
An l Association; died June 10, aged 83, of arterio-
scle

Skogen, Thomas T., Dell Rapids, S. D.; Minneapolis College of Physicians and Surgeons, Minneapolis, 1900; served as mayor of Flandreau; died in Duluth, Minn., June 22, aged 91, of carcinoma of the prostate with metastases.

Sloan, Edgar Hamlin, Ben Avon, Pa.; Baltimore Medical College, Baltimore, 1898; veteran of World War I; served as a member and president on the staff of the Suburban General Hospital in Bellevue; last June was given an honorary degree of doctor of laws by Geneva College, Beaver Falls; an associate member of the American Medical Association; died July 16, aged 86, of coronary occlusion.

Smith, Darwin Elbert ⊕ Corbin, Ky.; Medical College of Virginia, Richmond, 1938; member of the American Academy of General Practice; veteran of World War II; on the staff of the Southeastern Kentucky Baptist Hospital, where he died April 29, aged 46, of coronary occlusion.

Smith, Gideon Davis, Kenmore, N. Y.; Niagara University Medical Department, Buffalo, 1896; an associate member of the American Medical Association; on the courtesy staffs of the Millard Fillmore and Kenmore Mercy hospitals in Buffalo; died in Bluff Point July 18, aged 83, of coronary occlusion.

Smith, Greene Hampton, Sr. ⊕ Birmingham, Ala.; University of Tennessee College of Medicine, Memphis, 1916; member of the American Academy of General Practice; veteran of World War I; on the staffs of the Birmingham Baptist Hospital and the Jefferson-Hillman University Hospital, where he died June 6, aged 67, of brain tumor.

Smith, John Edward Vincent, Bayville, N. Y.: New York Homeopathic Medical College and Flower Hospital, New York City, 1934; veteran of World War II; physician for the fire department; on the staff of the Huntington (N. Y.) Hospital; died in the Veterans Administration Hospital, Brooklyn, July 16, aged 47, of Laennec's cirrhosis.

Smith, Paul Elmer ⊕ Bloomington, Ind.; University of Kansas School of Medicine, Kansas City, Kan., 1934; formerly on the staffs of the New Jersey State Hospital in Trenton, and the Richmond (Ind.) State Hospital; died Aug. 26, aged 53, of aortic stenosis.

Smith, Sigmund Ludwig ⊕ New York City; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1925; veteran of World War II; retired from the Veterans Administration Feb. 1, 1954; died July 2, aged 53, of myocardial infarction.

Spencer, Harvey ⊕ Ann Arbor, Mich.; Yale University School of Medicine, New Haven, Conn., 1924; certified by the National Board of Medical Examiners; member of the American Psychiatric Association; associate psychiatrist, health service, University of Michigan; formerly staff psychiatrist at the Austen Riggs Center in Stockbridge, Mass., where he was trustee and vice-president of the public library; died in the Massachusetts General Hospital, Boston, July 11, aged 59.

Spurgeon, Leota, Tipton, Ind.; Indiana University School of Medicine, Indianapolis, 1911; died June 27, aged 73, of congestive heart disease and arteriosclerosis.

Stankus, Ignatius John, Philadelphia; Indiana University School of Medicine, Indianapolis, 1910; an associate member of the American Medical Association; died in St. Agnes Hospital July 22, aged 81.

Stansbury, Eugene Milton, Vermillion, S. D.; University of Nebraska College of Medicine, Omaha, 1909; member of the South Dakota State Medical Association and the American Academy of General Practice; professor of obstetrics and gynecology at University of South Dakota School of Medical Sciences; veteran of World War I; died July 18, aged 75, of coronary disease.

Stokey, Fred Eicher, South Hadley, Mass.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, Chicago, 1912; retired medical missionary; veteran of the Spanish-American War; died July 14, aged 76, of acute coronary thrombosis.

Stoll, Harry J., Wooster, Ohio; Rush Medical College, Chicago, 1900; fellow of the American College of Surgeons; on the staff of the Wooster Community Hospial; died July 22, aged 80.

Sullivan, Dennis William ⊕ Lieutenant Colonel, U. S. Army, retired, Santa Monica, Calif.; Ensworth Medical College, St. Joseph, Mo., 1911; veteran of World War I; entered the medical corps of the U. S. Army in 1920; became a lieutenant colonel in 1937; retired April 30, 1942; died in the Veterans Hospital Center in Los Angeles June 2, aged 73, of mediastinitis with empyema due to perforated esophageal peptic ulcer.

Svoboda, Joseph Edward, Cleveland: Ohio State University College of Medicine, Columbus, 1928; veteran of World War II; on the staffs of St. Ann Hospital and St. Alexis Hospital, where he died July 28, aged 58, of carcinoma of the colon.

Sweet, Robert Ballantine, Fullerton, Calif.; Rush Medical College, Chicago, 1902; specialist certified by the American Board of Otolaryngology; fellow of the American College of Surgeons; veteran of World Wars I and II; died in the Veterans Administration Hospital, Long Beach, July 10, aged 79.

Terrill, Elwyn Eugene ⊕ Los Angeles, Calif.; College of Medical Evangelists, Loma Linda and Los Angeles, 1927; member of the American Academy of General Practice; on the staff of the California Hospital; died July 30, aged 55, of cancer of the liver.

Thometz, Alan Frederick ⊕ Glenview, Ill.; Northwestern University School of Medicine, Chicago, 1947; interned at the Cook County Hospital, Chicago; formerly a resident at the Veterans Administration Hospital in Hines; service with the U. S. Public Health Service terminated Nov. 29, 1949; died in the Resurrection Hospital in Chicago Aug. 4, aged 33, or coronary thrombosis.

Thompson, Charles Edward Percy ⊕ Fairhaven, Mass.; Boston University School of Medicine, 1903; formerly on the Fairhaven School Committee, school physician, and on the board of health; a member of the associate staff of St. Luke's Hospital in New Bedford, where he died July 30, aged 76.

Thorn, Druery Rodgers ⊕ Kansas City, Mo.; Jefferson Medical College of Philadelphia, 1921; on the staffs of St. Luke's Hospital and Kansas City General Hospital, where he was at one time medical director; died Aug. 12, aged 63, of coronary occlusion.

Trainor, Joseph Aloysius ⊕ Cambridge, Mass.; College of Physicians and Surgeons, Baltimore, 1904; College of Physicians and Surgeons, Baltimore, 1905; died July 13, aged 80.

Turkel, Ashur Sigmund ⊕ Los Angeles; Stanford University School of Medicine, San Francisco, 1933; died July 14, aged 52, of coronary disease.

Walsh, Edmund A., Springfield, Ill.; College of Physicians and Surgeons of Chicago, 1897; served on the staff of St. John's Hospital, where he died July 21, aged 81 of grade 1-2 epidermoid carcinoma of the tongue.

Warren, Edward Crawford ⊕ Bay City, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1892; died in Vanderbilt Aug. 6, aged 86, of uremia.

Wiley, Harold Williams ⊕ Lansing, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1912; past-president of the Ingham County Medical Society; veteran of World War I; director of procurement and distribution of blood for the state health department laboratories; for many years on the staffs of the Edward W. Sparrow and St. Lawrence hospitals; died July 15, aged 67, of coronary occlusion.

Williams, Donald Lee ⊕ Garden City, Kan.; University of Kansas School of Medicine, Kansas City, 1953; interned at the University of Kansas Medical Center in Kansas City, Kan.; died in Greensburg July 25, aged 31, of injuries received in an automobile accident.

Williams, Pierce Lee ⊕ Cordele, Ga.; Atlanta College of Physicians and Surgeons, Atlanta, 1913; member of the American Academy of General Practice; past-president of the Crisp County Medical Society; on the staff of the Crisp County Hospital, where he died July 9, aged 68, of acute coronary insufficiency.

Zimmerman, Mason Woodward, Rydal, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1888; on the staffs of the Wills Eye Hospital and Germantown Dispensary and Hospital in Philadelphia; died Aug. 11, aged 96.

FOREIGN LETTERS

COLOMBIA

Medical Bibliography.—The Bogota medical group, Unidia (Unidad para Diagnostico y Tratameinto), has published a quarterly journal, *Unidia*, for the last four years. In the July, 1956, issue the Unidia librarian has indexed all the Colombian medical literature published during the first semester of 1956 in the 17 Colombian medical journals. The greatest number of articles were on gastrointestinal diseases, medical societies, medical education, gynecology, obstetrics, psychology, and pediatrics.

DENMARK

Activities of Danish Medical Association.—The central committee of the Danish Medical Association has classified its activities as national and international. The first category includes such standard problems as the dealings between hospital medical staffs and police anxious to get information about accident cases admitted to hospital and ethical limits of advertising. On the international level, the committee reports a request from the American Medical Association for advice on how the American tourist who falls ill while traveling in Denmark may secure the best medical care under the best conditions. The Danish Red Cross Society renders assistance in such cases. The British Medical Association requested information about the Association of Junior Physicians, a branch of the Danish Medical Association to which there is, apparently, no counterpart in England. The Norwegian Medical Association desired information about the study of the history of medicine with reference to the organization of a society devoted to this subject in Norway. The Danish Medical Association in turn requested reprints of articles on this subject from this new society in Norway. The Zim Israel Navigation Company, Limited, invited Danish physicians specializing in rheumatism and arthritis to visit the warm springs of Israel. The invitation was forwarded to four physicians. Another invitation came from the 58th German Arztetag in Baden-Baden. The Danish recipient of this invitation found himself the object of the warmest hospitality and profited greatly from the discussions.

BCG Vaccination of Newborn Infants.—Dr. F. Tudvad and coworkers (*Danish Medical Bulletin*, volume 3, July, 1956) reported that in 1950 large-scale BCG vaccination of newborn infants was carried out. All the mothers confined in a municipal maternity hospital were invited to have their babies vaccinated with BCG vaccine unless the babies were ill or premature; 1,330 babies were so vaccinated, and 829 served as controls. The vaccine was given by intracutaneous injection in the deltoid region within a few days of birth. Of the 1,330 babies, 710 were tested for the Moro reaction two months after vaccination; there was a negative reaction in only 5. A follow-up examination of 1,199 vaccinated babies revealed that abscesses had developed in 33 of them (2.75%) within a year of the vaccination. This abscess rate was higher than that for children vaccinated with BCG at a later age. In other respects the outcome of this experiment was favorable to the vaccinated infants in respect of gains of weight. The data collected by the authors of this report failed to give a clear answer to the question of whether the tuberculin positivity conferred by the BCG vaccination of the newborn infant lasts as long as or longer than that conferred by the BCG vaccination of older children.

In *Ugeskrift for læger* for Aug. 9, Dr. E. Groth-Petersen says that, in principle and in order to be consistent, he favors BCG vaccination at birth, but in practice such vaccination presents difficulties of technique and complications are more frequent than with older children. The risk of accidental infection of the newborn infant with virulent tubercle bacilli is comparatively small. Because there is such a risk, however, most Danish phthisiologists prefer to reserve BCG vaccination of the newborn infant for special cases only, but every child who is tuberculin-negative when one year old should have the benefit of this measure. To emphasize the importance of this advice, the author points out that the overwhelming majority of the 350 children found in Denmark to be suffering from tuberculosis in 1954 and 1955 were below school age.

A Lifelong Investigation of Twins.—In the *Danish Medical Bulletin* for August, Harvald and Hauge gave a preliminary report on an investigation of nonselected twins. Of a total of 9,360 pairs of twins born in Denmark in the period 1870 to 1910, 1,900 were thoroughly investigated, a questionnaire being addressed to each twin (or in the case of death to the nearest relative) seeking information about a variety of conditions and the incidence of a long list of diseases. With regard to the 143 cases of tuberculosis (incidence 3.8%), concordance was nearly twice as great for uniovular as for binovular twins. This does not necessarily prove that tuberculosis is a hereditary disease, for the concordance found may simply reflect the fact that uniovular twins have a greater chance to infect each other than binovular twins have. Tuberculosis was the only infectious disease concerning which sufficiently accurate information was obtained on the score of heredity and other problems. The authors hope to treble their present material. When their compilation is completed, they hope to analyze the influence of hereditary factors on the expectation of life. Their preliminary rough estimate suggests that the influence of heredity is minimal compared with environment. They also hope to make an estimate of the influence of heredity on twinning, and on twinning in relation to crime.

Complications of Diabetes Requiring Surgery.—Because of use of insulin and the rise in life expectancy, diabetics now represent 0.5% of the total population of Denmark. On the other hand, the indications for operation have been broadened due to recent advances in medicine. Dr. Knud D. Carlsen in *Ugeskrift for læger* for Aug. 23 states that about half of the diabetics now operated on for their complications have had the disease for more than 15 years. Consequently many of them also suffer from serious deterioration of their cardiovascular systems. At the Aarhus City Hospital, diabetics with complications requiring surgery enjoy the benefits of close cooperation between surgeons, physicians, and anesthetists, whose teamwork is reflected in a falling operative and postoperative mortality. In 1938 and 1939, 49 diabetics in this hospital were treated surgically for complications. In the two-year period ending July 31, 1955, 81 were treated for such complications. In both groups the diabetics represented 0.7% of the hospital's patients. Broadly speaking, the mortality was reduced so effectively that in the second period it was only 33 to 50% of what it had been in the first.

Dumping Syndrome.—Dr. H. K. Lassen (*Ugeskrift for læger*, Aug. 30, 1956) reports a series of 163 patients (147 men and 16 women) who had had a gastrectomy. Follow-up revealed that 86 were well; 61 had only slight discomfort; and 16 (15 men and one woman) had a poor result. Lassen could not explain why some patients in his series suffered from the dumping syndrome (36%) and loss of weight (42%), while others did not. The patients were classified in three groups, according to whether they had done heavy or light work or none at all, but none of these groups was distinguished by any marked difference in the recovery rate. In the same issue an editorial states that in the last 10 or 15 years there has been a growing tendency to favor the operative treatment of gastric and duodenal ulcers because of an operative mortality of less than 1%, the good operative results, and the discovery that the results of medical treatment are worse than anticipated. It is, however, common practice to

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The items in these letters are contributed by regular correspondents in the various foreign countries.

await the results of two courses of medical treatment before considering operation. Negative radiological findings should be a contraindication to operation, even if symptoms have persisted for years, but, if the distress becomes intolerable, it may be permissible to operate in the face of negative radiological findings, as a low-level duodenal ulcer may have not been visible on the roentgenogram. Gastroenterostomy is less in favor than formerly because the ultimate results have been disappointing. This observation does not apply to patients over 60 years of age.

FRANCE

Epidemic of Typhoid.—At the meeting of the Medical Society of Paris Hospitals on June 22, Ferrabouc and Bernard presented an account of a typhoid epidemic starting on Jan. 15, 1954, in Lyon and involving 158 young soldiers in a garrison of 2,327. One patient died. This was one of the largest epidemics occurring in the army in peacetime. Of the 158 patients, 137 had been vaccinated. The authors suggested that an attempt be made to heighten the immunity of the soldiery by increasing the number of vaccinal injections from three to four. This method was successful in another garrison in controlling an epidemic of salmonellosis due to Salmonella schottmülleri.

Hypophysectomy for Cancer of the Breast.—At the June 29 meeting of the same society, D. Lebeau and co-workers reported on a series of 25 patients who had undergone hypophysectomy for cancer of the breast. They concluded that (1) the operation is contraindicated in patients with hepatic metastases, but it is indicated in those with metastases to the bones or lungs, (2) if each patient's condition is satisfactory before the operation the case fatality rate is small thanks to preoperative and postoperative treatment with cortisone and corticotropin, and (3) in 90% of the patients who have hypophysectomies the pain is immediately relieved. Results observed in patients with cancer of the prostate, testis, or uterus were not as good.

Hepatic Siderosis.—At the same meeting J. Lereboullet and co-workers reported the frequency of hepatic siderosis in alcoholics based on the findings of 270 autopsies and 80 specimens from needle biopsy. They observed a deposit of iron in the livers of 66% of the patients with cirrhosis, 58% of the patients with precirrhotic conditions, and 59% of the alcoholics. In all patients with hepatic siderosis the authors found an excess of iron pigment in such organs as the spleen, pancreas, myocardium, kidney, and testis. They found that the proportion of patients with nervous manifestations who had siderosis was greater than that of those without nervous manifestations. Of 20 patients with delirium tremens they found iron in 80%; of 10 patients with alcoholic encephalopathies they found iron in 80%; and of 14 patients with polyneuritis they found iron in 75%.

Treatment of Trichomoniasis.—At the meeting of the French Society of Gynecology, Carcia reported that a series of 80 patients whose vaginal discharge contained Trichomonas vaginalis was treated with two to eight insufflations of ozone into the cervical canal and the vagina. In all patients the leukorrhea, vaginitis, and trichomoniasis disappeared. In 55, two or three insufflations were enough. Ozone is harmless to the tissues, acts as a deodorant, and is strongly bactericidal.

Prednisone in Dermatology.—In *La presse médicale* (June 23, 1956) E. Sidi states that prednisone applied locally does not give better results than cortisone. He gave prednisone by mouth to 101 patients suffering from eczema, generalized psoriasis, pemphigus, and erythroderma ichthyosiforme congenitum. The clinical results were good, 80% of the patients showing improvement. The drug is indicated in the treatment of pemphigus, acute lupus erythematosus, and other acute dermatoses. In half of the patients receiving a dose of 20 mg. per day edema appears, the serum potassium level drops, and psychic disturbances are likely to occur. Treatment with this drug should not be suddenly discontinued.

INDIA

Effect of Chlorpromazine in Aminopyrine-Induced Analgesia.—M. L. Gujral and co-workers (*Journal of the Indian Medical Profession*, August, 1956) state that, since chlorpromazine is alleged to enhance the analgesic effects of morphine, meperidine, and aspirin, they have studied its effect on analgesia induced by aminopyrine. Albino rats were divided into four groups of 10 each. Each group was given a dose of a drug, combination of drugs, or placebo and tested for analgesia. The groups were rotated at intervals of one week and at the end of the experiment all the animals had received the same tests. Chlorpromazine was found to enhance the analgesic effect of aminopyrine. There was no change, however, in the time of peak effect and duration of analgesia.

Diagnosis of Leprosy.—Nerurkar and Khamolkar (*Indian Journal of Medical Research*, July, 1956) state that millions of acid-fast bacilli can be easily demonstrated in every microscopic field of a smear prepared from a lepromatous skin. It is, however, difficult to find these organisms in a smear from a patient suffering from the tuberculoid type of leprosy, and still more difficult to demonstrate the organisms in contacts of leprous patients or in smears of patients after treatment with sulfones. Routine skin smears from such patients almost always give negative results. In 1952 a different technique of concentration of leprosy bacilli was made available. The authors used fluorescence microscopy on 20 subjects (18 patients with tuberculoid leprosy and 2 contacts without any clinical signs of this disease). Of the 18 patients, one was treated with diaminodiphenylsulfone for about five years. Acid-fast bacilli were found in all these patients without difficulty. As a control, skin biopsy specimens were obtained from persons who attended the hospital for minor injuries. None of these showed acid-fast bacilli. The advantages of the method are that (1) the pressure mincer, being hand operated, can be used in any part of India even when electricity is not available; (2) crushing of the tissue is thorough and easy; and (3) the fluorescing organisms are more easily seen against a partially dark background than with the Zeihl-Neelsen staining method and there are therefore fewer chances of missing isolated organisms.

World Health Day.—April 7 this year was devoted to educating the public regarding the eradication of insect-borne diseases. Local chapters of the Indian Red Cross enthusiastically supported the public health authorities and the World Health Organization in conducting campaigns throughout the country. They organized public meetings, exhibited health films, and participated in disinfecting wells and other mosquito breeding places. Pamphlets on insect vectors were freely distributed.

Response of Guinea Pigs to Histamine Aerosol.—M. L. Gujral and co-workers (*Journal of Postgraduate Medicine*, July, 1956) reported their observations on the relative potency and duration of action of antihistamines by exposing guinea pigs to histamine aerosol. They found that a previous exposure to histamine aerosol does not significantly influence the response of guinea pigs subjected to a second exposure three hours later. The amount of histamine required to produce bronchoconstriction when histamine was given by aerosol was found to be a very small fraction of the intravenous lethal dose. An occasional animal was found to have a refractory response to histamine aerosol and such animals were dropped from the test groups. Attempts to reproduce narcosis, which has been reported after intracardiac injection of histamine, by intraperitoneal injection ended in failure. Large doses resulted in gastroduodenal ulceration and sometimes perforation.

Response of Endocrine Glands to Irradiation.—T. C. Wasson, in the *Journal of the Indian Medical Association* (Aug. 16, 1956), says that radiotherapy of the endocrine glands is cheap and safe, and elicits a quick response. The technique is simple and requires no hospitalization or after-care. Radiosensitivity differs from gland to gland and in the same gland at different times.

The variation is directly proportional to the functional activity of the cells. The pancreas and adrenals are unsuitable for radiotherapy, as they are surrounded by tissues that are more radiosensitive, and, therefore, their exposure to the action of x-rays cannot be undertaken without damaging the surrounding tissues. The pituitary, thyroid, ovary, breast, and thymus glands can be irradiated without harm. These glands during their periods of normal activity are radioresistant and become radiosensitive only when their functional activity is accelerated. During this stage irradiation will curb their activity and bring it down to normal. Hypofunctioning of a gland is a complicated phenomenon. It is chiefly due to surgical excision, tumor formation, or a cause that reduces the number of secreting cells. It is therefore not possible to make up the deficiency of the quantity of the hormone by stimulation of the remaining cells. On the other hand, if the secreting tissue is not reduced and the deficiency is purely functional, small doses of x-ray do stimulate the glands. In young girls approaching puberty, one small dose given for early, scanty, or painful menstrual periods will produce the desired effect. Hypofunction of the testes is invariably secondary to hyperactivity of the pituitary and thyroid glands, and their irradiation therefore has a favorable influence on the testes.

Peptic Ulcer.—Mukherjee and co-workers (*Journal of the Indian Medical Association*, Aug. 1, 1956) noted an increase in the incidence of peptic ulcer in West Bengal in recent years. Men in the fourth decade of life comprised the largest percentage of the patients, and the role of stress was evident in the pathogenesis of the disease. In the authors' series of 82 patients, all had duodenal ulcer. Some were treated with a new anticholinergic drug, oxyphenonium bromide, and preliminary observations suggest that, without an antacid supplement, the drug, given in doses ranging from 15 to 60 mg. in 24 hours according to severity of symptoms, produces beneficial effects clinically as well as radiologically in three weeks' time. Relatively few side-effects were observed.

NORWAY

Lung Cancer and Smoking.—Two articles in *Tidsskrift for den norske lægeforening* for Aug. 15 approach lung cancer from somewhat different angles. Dr. Roald Opsahl emphasizes the comparative rarity of primary lung cancer in Norway between 1916 and 1935, during which period, of 2,005 cases of cancer verified by postmortem examinations, only 56 were primary cancer of the lung. These were equally divided between the sexes and included only two patients in whom there was a record of heavy smoking. After pointing out that the death rate from lung cancer has tripled in Norway in the last two decades, Opsahl censures the government on the score of its passive attitude toward cigarette smoking, from which it derives a certain revenue. He also deplores the failure of the National Cancer Association to wage a more vigorous campaign against the inhaling of cigarette smoke. The other article, by Dr. Einar Pedersen, draws attention to the fact that Norway and Denmark are at present the only countries in the world in which a scheme has been adopted for the systematic review of death certificates in order to examine the diagnoses of lung cancer. Thus, in 1953 there were 209 cases originally so diagnosed in Norway, but, on review, 24 of these diagnoses had to be altered. The author further states that in 1930 only 0.9% of all the deaths from cancer in Norway were due to cancer of the respiratory tract, whereas the corresponding figure for 1952 was 3.6%. Up to 1954, the rise seems to have been limited almost exclusively to the urban male population, and for this group the rise has been and still is great. There is also a tendency for the peaks of the age curves for successive years to shift toward older age groups.

The Dangers of Prolonged Pregnancy.—In August the Northern Association for Obstetrics and Gynecology met in Oslo. The first subject dealt with was prolonged pregnancy, the sinister significance of which has been preached for many years by Dr. K. Skajaa, who is in charge of the Oslo Municipal Maternity Hospital. The present-day teaching that the infant mortality rate at birth rises from 1% when pregnancy has lasted the normal 280 days to 4% when it has lasted 294 days or more is a tribute to Skajaa's pioneer work in this field. A study (*Acta obstetricia et gynecologia scandinavica*, volume 35, part 2, 1956) by Dr. Arne Strand states that in the period 1918 to 1929 no special consideration was given to prolonged pregnancy. This period was compared with that between 1947 and 1955 when special attention was paid to this problem. A series of 10,151 deliveries was studied. In the first period 3,288 patients and in the second 2,092 were primiparas. The outcome of a confinement was influenced by the age of the mothers, whether they were primiparas or multiparas, the duration of the pregnancy, the weight of the infants at birth, and other factors. Primiparas 35 years of age or older showed a greater tendency to prolonged pregnancy than those who were younger. The rates for antenatal, intranatal, and postnatal infant mortality rose with the duration of pregnancy after it had lasted 280 days, and this was particularly the case with primiparas. Strand concludes that the induction of labor at term, after critical evaluation of each case, appeared to have reduced the perinatal death rate, that complications are not more serious after induced than after spontaneous labor, and that the speedy induction of labor is the best treatment after the indications for it have been determined.

PORTUGAL

Sickling of Erythrocytes.—Leite and Ré (*Arch. Inst. Pasteur Algérie* 33:344, 1955) studied the sickling of erythrocytes in the Portuguese African province of Guinea. This province has many tribes, including Melano-Africans and Ethiopians. These tribes do not mix, and, going from the coast to the interior, one finds a stratification in the distribution of tribes, resulting from the successive original invasions. The authors investigated the percentage of sickle cells in blood samples from random groups in each native tribe. About 6,000 blood specimens were examined. The highest values (17 to 23%) were found in the last invaders of Guinea (Mandinga and Fula tribes) and the lowest (1.7 to 8.3%) in the aboriginal populations. The authors believe that a high percentage of sickle cells is not a common characteristic of all African Negro populations, as others have stated, but a peculiarity of the later invaders of the African continent, who probably came through Ethiopia. An important confirmation of this view was found in another investigation by these authors. They investigated in the interior of Angola a tribe of Bochiman, surely the oldest invaders of the African continent, who are still free from hybridization, and, among 249 natives, they did not find a single case of sickling.

Yellow Fever.—Cambournac and co-workers (*An. Inst. med. trop.* 12:101, 1955) collected blood in 61 zones of Angola, mostly from 1,549 children under 15 years of age, and performed the neutralization test for yellow fever virus in mice. Only 38 specimens were positive. The authors believe that the positive results obtained in the north inland and coastal regions of Angola are probably due to the presence of the yellow fever virus there but that the scarcity of positive results found on the southern frontier might have been due to vaccination of the natives. In the north the many rivers, bordered by dense forests; the long rainy season (six to eight months); and the great number of monkeys make eradication of the virus difficult.

SWITZERLAND

Prednisone in Treatment of Malignant Lymphomas.—At the Medical Clinic of the University of Geneva, Dr. Dubois-Ferrère and co-workers have treated adults with acute leukemia with large doses (1 to 2 gm. daily) of cortisone. This treatment was continued for 8 to 21 days. More recently they have used prednisone in daily doses of 1 gm. and have observed a rapid and sometimes amazing regression of adenopathies and of parenchymatous and pleural effusions, sometimes amounting to complete disappearance of all roentgenologic signs. Although recurrence can be expected, the relief while it lasts is most gratifying.

Poliomyelitic Antibodies.—R. Martin-Du-Pan and co-workers have studied the poliomyelitic antibodies in 163 normal persons of all ages living in Geneva and coastal communities, particularly in families of pediatricians. The authors do not believe that the presence of antibodies in the serum means total immunity. They observed that the percentage of patients showing antibodies in their serum increases steadily beginning with those 6 months old. They further concluded that immunity of the population of Geneva is about the same as that of Switzerland as a whole. The children of pediatricians and physicians working in virus laboratories showed no greater antibody titer to poliomyelitic antigens than did other children living under similar conditions. This may be explained by the fact that physicians and other persons who have greater than average contact with poliomyelitis virus take precautionary measures to avoid infection.

UNITED KINGDOM

Pertussis Vaccine.—A further report on the results of vaccination of children against pertussis was made by a group of workers appointed by the Whooping Cough Immunization Committee of the Medical Research Council (*Brit. M. J.* 2:454, 1956). Two series of field trials were made in which 28,799 children were followed up for an average of two years after inoculation with pertussis vaccine. Severe local or general reactions were not encountered, and there was insufficient evidence to show that pertussis vaccine precipitated convulsions or initiated serious cerebral damage. In three cases of poliomyelitis occurring within 28 days after injection of the vaccine, paralysis was confined to the limb injected. Two types of vaccine were used, one from 24-hour or 48-hour cultures of a single strain on Bordet-Gengou medium containing horse blood, the other from culture in liquid medium. Formalin was used as a bactericide and phenol or thimerosal as a preservative. This vaccine gave poor protection. Another vaccine was made from a mixture of four, six, or seven freshly isolated strains that had been subcultured on very few occasions before being freeze-dried. Three types of vaccine were made with Bordet-Gengou medium containing sheep's blood, human blood, and a liquid medium respectively. All were killed and preserved with thimerosal. Field studies showed that three of five batches of this second vaccine were as effective as a reference vaccine made with American strains and supplied by the Michigan Department of Health and that the vaccine prepared by the State of New York Department of Health from the same American strains as the reference vaccine, but grown in a liquid medium, was as effective in a preliminary trial as the reference vaccine. While the clinical trials were in progress, laboratory tests were made to determine the ability of the vaccines to protect mice against intracerebral pertussis infection. There was a correlation between protection in children against pertussis and the three following laboratory tests: protection of mice against intracerebral infection with Hemophilus pertussis, production of a specific agglutinin in mice, and production of a specific agglutinin in children. It does not necessarily follow that the laboratory tests measure directly the factor or factors responsible for the production of immunity in children. Agglutinin production in children has been accepted by some workers as evidence of protective potency, and the tests reported by the committee support this conclusion. As it would hardly be practical to test each batch on children, the mouse intracerebral test is considered to be the most satisfactory one. A British standard pertussis vaccine has been established in terms of which other vaccines may be assayed. It is freeze-dried in a 6% dextran solution. The committee considers that, before a pertussis vaccine is issued, it should be submitted to the mouse intracerebral protection test to ensure adequate potency.

Carbutamide and Diabetes.—Carbutamide is used orally for the treatment of diabetes (*British Medical Journal*, Aug. 25, 1956). Trials were organized in six centers in England and Scotland on a total of 193 inpatients and outpatients. The results confirm the German observation that the type of patient that responds best to this drug is the middle-aged or obese diabetic who has never been ketotic and who needs less than 30 units of insulin daily. In general, grossly obese diabetics were not included in the trial. All groups carrying out these investigations concluded that, in the right type of diabetic, carbutamide, in doses of 1 to 4 gm. daily, reduces the blood sugar level to within normal limits for most of the day. It does not affect glucose tolerance or have any influence on the postprandial rise in the blood sugar level, and, contrary to the view expressed in Germany, treatment must be continuous and not intermittent. The drug is without effect on diabetic ketosis or in patients who rapidly develop ketosis or even have acetonuria. The fasting blood sugar level appears to be an important factor in assessing the effect of the drug. If this is more than about 275 mg. per 100 ml. after insulin administration has been stopped, the drug is not likely to be of value in producing a normoglycemia. The reports emphasize the danger of withdrawing insulin in apparently suitable persons with stable diabetes not apparently liable to ketosis. Several such patients developed severe diabetic ketosis within a few days when given carbutamide. This shows that, if a diabetic receiving insulin is transferred to treatment with the new drug, he must be seen daily or hospitalized after the insulin administration is stopped.

Diabetics in whom carbutamide failed had higher insulin requirements than those who responded. If insulin is essential for treatment, then any attempt to replace it by carbutamide will result in a serious relapse. Response nearly always occurred in patients whose diabetes commenced after the age of 40 years. Studies of arteriovenous blood sugar differences and of the changes in serum inorganic phosphorus level provided no evidence that the new drug increased the effectiveness of the peripheral action of insulin. Carbutamide is ineffective in patients suffering from sepsis. Diet remains the mainstay of treatment for the middle-aged diabetic, and carbutamide is only indicated in a comparatively small group. Although it may control the blood sugar level, the British clinicians are concerned about the development of retinitis and nephropathy. Will the drug control these? A most disturbing feature of the reports is the high incidence of side-effects. The incidence of sulfonamide rash was 9%; persistent neutropenia occurred in a number of patients; and hypothyroidism, drug fever, and depression of blood platelets with purpura were reported. Carbutamide is, therefore, a dangerous substance, unsuitable for the long-term control of mild diabetes and definitely unsuitable for those diabetics needing insulin. It may even cause fatal granulocytopenia and thrombocytopenia and should be used only under the most careful medical supervision.

Explosions in Operating Rooms.—In 1953, the Ministry of Health appointed a committee to investigate anesthetic explosions. The conclusions of the committee (Report of a Working Party on Anesthetic Explosions, London, Her Majesty's Stationery Office, 1956) are based on 36 such explosions. Most of these could have been avoided if the possibility of explosion had been borne in mind and if every hospital had taken routine precautions. Most explosions are due to static electric discharges. It is difficult to ensure that conditions are such that these discharges cannot occur, but if the necessary precautions are taken the chances of an explosion occurring are rare. Most of the explosions investigated were attributed to the use of nonconducting rubber. The routine use of antistatic rubber would eliminate explosions due to static discharges. As soon as reasonable standards for such rubber can be laid down, the Ministry of Health should equip operating rooms with it without delay. It would be a comparatively small item in the hospital budget. Another source of explosions is the use of nonconducting footwear by operating-room personnel. Overshoes should have antistatic rubber on the under surface. Gowns should be made of antistatic fabric tied loosely to reduce the generation of an electric discharge in the clothes beneath. Woolen blankets should not be brought into the operating room, as they may become readily electrified.

Only 5 to 10% of operating rooms in Great Britain have nonconducting floors (rubber or cork). In operating rooms without such floors the danger of explosion can be decreased by dampening the floor or by putting a damp sheet down if evaporation is rapid. If explosive anesthetics are used routinely, the only safe procedure is to lay a new, nonconductive floor. The use of nonconducting paints for floors is being investigated. The best measure to reduce the danger of static discharge is to maintain a high humidity. Most of the explosions occur in abnormally dry weather. All operating rooms should therefore be equipped with an instrument measuring humidity and with a device for increasing it when necessary. It should be the duty of one of the operating room attendants to warn the anesthetist when humidity drops below 50%. An apparatus that ionizes the air so that charges are quickly dissipated is now available, and the committee would like to see how effective it is as an antistatic device. The physiological effects of breathing ionized air should also be investigated. The only sure method of preventing hospital explosions at present is to eliminate all explosive anesthetic agents. The use of substances rendering explosive gases noninflammable should be investigated. Such a substance is commercially available for making gasoline noninflammable. The use of noninflammable xenon and fluorine-substituted anesthetics, which are noninflammable, should be investigated. The report emphasizes that all persons employed in the operating room should be made explosion-conscious.

Cancer and Leukemia in Children.—Health departments all over Great Britain are engaged in an environmental survey that will eventually cover about 1,500 children who died of leukemia or cancer before the age of 10 between the years 1953 and 1955. A preliminary report was made by Dr. Stewart and her co-workers in the department of social medicine, Oxford. Where possible, radiological data are checked from hospital records and the details are noted of the mother's health before and during the relevant pregnancy and of any irradiation, for either diagnostic or therapeutic purposes, that she may have received during pregnancy. A note is also made of any case of malignant disease in the family, any degree of consanguinity between parents and grandparents, and certain features of the child's diet and home environment. Similar data have been collected from control children of the same age and sex living in the same district. One reason for attempting this nationwide survey was the possibility that the peak of leukemia mortality in early life might be explained by the action of weak irradiation initiating malignant changes in a fetus or a very young child. From the figures collected so far it appears that the number of mothers of leukemic children who had a radiological examination of their abdomen during the relevant pregnancy was twice that of the mothers of the control children. This was also true for the mothers of children dying from malignant disease. It has also been established that the dose of irradiation received by the fetal gonads frequently exceeded 2.5 r. The present investigation suggests that, besides causing genetic damage, diagnostic radiology during pregnancy may occasionally cause leukemia or cancer of the unborn child.

A New Syndrome.—Baron and co-workers (*Lancet* 2:421, 1956) have described a new syndrome, characterized by a rough, reddened skin on exposure to light similar to that seen in pellagra, a severe but reversible cerebellar ataxia, renal aminoaciduria, a constant large urinary excretion of indole-3-acetic acid, and an increased quantity of protoporphyrin in the feces. This new disease affected four of eight children of a first-cousin marriage. It was thought that the condition might be a disorder of tryptophan metabolism, whereby a metabolic block exists somewhere along the pathway from tryptophan to nicotinic acid. Another possibility is that the syndrome might be caused by a conditioned nicotinic acid deficiency due to the diversions of tryptophan from its normal metabolic pathways into the pathways of indican and indolacetic acid formation. All the patients were children. In this disease there may be a variation with age and stress in the requirement for endogenous nicotinic acid, which would explain the clinical deterioration with growth and infectious disease and the possible later improvement in adult life. The renal aminoaciduria was attributed to the poisoning of the kidney tubules by an abnormal indole metabolite. It could also be explained by a primary disorder of amino acid transport processes leading to an abnormal intestinal flora that distorts the normal sequence of nicotinic acid metabolism.

Changing Dietary Pattern.—The latest report on food consumption in Great Britain, issued by the Ministries of Agriculture, Fisheries, and Food (Domestic Food Consumption and Expenditure—1954: Fifth Annual Report of the National Food Committee, London, Her Majesty's Stationery Office, 1956) shows that the pattern of the national diet is changing. The year 1954 was a year of transition from a controlled to a free economy. Before then, meat, fats, and cheese were still rationed and subsidized by the government, but by July, 1954, all direct controls had ended and the only remaining subsidized foods were bread, milk, and welfare foods (dried milk, cod liver oil, and orange juice). By 1954, expenditure on food by the population rose more than food prices and a larger share of the national income was being spent on food. As a percentage of total expenditure on consumers' goods and services, expenditure on food rose steadily from 29.8% in 1938 to 32.1% in 1954, and the daily caloric consumption increased from 3,000 to 3,130. Because this is caloric consumption "as bought" and not "as consumed," allowance must be made for wastage in preparation and cooking. Consumption has risen in all the main food groups except cereals, potatoes, and other vegetables. For meat it rose 12%, for fat and oils 7%, and for sugar and syrup 8%. The decline in cereal consumption has been continuous and is associated with a rising standard of living. Milk consumption has also increased, but that of fish has decreased. The weekly per capita consumption of milk, both fresh and processed, is 5.1 pt. The percentage of calories derived from animal sources has risen steadily to 54 and that of fat to 36.5. In those households with a yearly income of more than $2,500, 40% of the calories of the diet come from fat, 48% from carbohydrate, and 12% from protein.

Certain foods show a class gradient. Thus the consumption of protein, fat, iron, vitamin A, riboflavin, and ascorbic acid is directly proportional to the income of the family, but, except for iron in the low income groups, the intake of the other nutrients is above the recommended allowances of the British Medical Association's committee on nutrition. The diet of the family with a large number of children contains more bread, potatoes, and milk, about the same amount of sugar, but less meat, cheese, fish, fruit, and green vegetables than the diet of the average childless couple. Although the difference between the nutritional standards of households with and without children has widened, it is due not to deterioration of the diet of the large family but to the improvement of that of the small family. The greatest dependence on carbohydrates as a source of energy was found in households with four or more children or with children and adolescents. In families of three children protein consumption is 92% of that recommended by the British Medical Association nutrition committee; in families with four or more children it is 87%. These figures would be higher if a lower extraction rate were used by the millers in the preparation of white flour.

Hunters' Birthplace.—A committee representing the University of Glasgow, the Royal Faculty of Physicians and Surgeons, Glasgow, and the East Kilbride Development Corporation has been organized to raised a fund for the renovation and preservation of the birthplace of William and John Hunter at Long Calderwood in Scotland. A sum of $56,000 is required to restore the fabric of the house and provide an endowment fund for future maintenance; $8,500 has already been raised in Scotland. The committee plans to organize a board of trustees to maintain the house as a memorial, a museum, a place of pilgrimage, and, if sufficient money is forthcoming, a research center. An appeal is being made to all members of the medical profession "to save this national historic monument as a fitting memorial to the two brothers whose names will ever be gratefully remembered for their unique achievements in the advancement of medical knowledge."

High-Energy Radiation Unit.—A new high-energy radiation treatment unit has been opened at Cookridge Hospital, Leeds, and is being developed as a regional radiotherapy center. Funds for this have been provided by the Rockefeller Foundation, the British Empire Cancer Campaign, and the Leeds Regional Hospital Board. The new unit is the first of its kind in the country, as it will combine radiotherapy and radiation research. It shares with the British Empire Cancer Campaign the largest therapeutic source of radioactive cobalt in the country. The unit has been planned to provide new techniques for the treatment of cancer and for research on the physical, chemical, and therapeutic action of high-energy radiation. Physicists, chemists, and radiotherapists will work in collaboration under one roof. The source of high-energy radiation will emit radiation equivalent to a machine working at about 3 million volts.

CORRESPONDENCE

CANCER AS A CAUSE OF DEATH AMONG PATIENTS WITH OTHER CHRONIC DISEASES

To the Editor:—Doshay (*J. A. M. A.* 156:680-684 [Oct. 16] 1954) has suggested that patients with paralysis agitans are less likely than others to contract cancer. He states: "For reasons as yet unclear, cancer is phenomenally rare in paralysis agitans, despite the fact that the patients are in the age group 45 to 75, when the expectancy of cancer in the general population is high. Only one proved instance of cancer has developed among the several thousand cases I have followed during the past 20 years, and this patient had a rectal cancer, without operation or metastases, for 5 years, until she died during a vascular episode."

The patient material from the Ullevål Hospital (Oslo City Hospitals) has been used in an attempt to study this point quantitatively. All patients discharged alive during the years 1917-1950 with a diagnosis of paralysis agitans or Parkinsonism, a total of 154, were registered. One record could not be located. The records for the other patients were studied, and each record was placed in one of the following four groups: (1) typical paralysis agitans without known etiology, 90 records; (2) postencephalitic Parkinsonism, 16; (3) doubtful paralysis agitans, 40; and (4) probably not paralysis agitans or postencephalitic Parkinsonism, 7. The seven cases in group 4 were omitted from further study. The remaining 146 patients were followed either until death or until July 1, 1955. One hundred eleven patients had died during the observation period, 31 were still alive at the end of the period, and 4 patients could not be traced. The total number of observation years in the material was 763.5. The expected number of deaths from cancer during these years was calculated in the following manner: Males and females were treated separately. The observation years were distributed in 10-year age groups and 5-year calendar year groups and multiplied by the corresponding official cancer death rates in Norway. These calculations gave a total of 3.6 expected cancer deaths in the material. Determination of actual deaths certified as due to cancer was obtained by studying the death certificates of the 111 patients who had died. In three cases the certificate could not be found. A total of seven deaths had been certified as due to cancer. Further information collected for these deaths revealed that the diagnosis had been confirmed by autopsy in two cases. In three other cases the diagnosis was built on reasonably conclusive examinations prior to death. In the remaining two cases the diagnosis was questionable. These results—7 actual deaths versus 3.6 expected—do not lend support to the hypothesis that patients with paralysis agitans are in any way protected from contracting cancer. It may be mentioned that, among the patients with typical paralysis agitans (group 1 above), there were 6 deaths due to cancer against an expected number of 2.0.

It might be said against the method here employed that persons with chronic diseases possibly stay more completely under medical control than the average population, so that cancer will be more frequently diagnosed. Although this probably will not be of any great importance, we thought it might be of interest to compare the actual and the expected number of deaths in patients with other chronic diseases. To do this, we have used the materials from follow-up studies in two groups of patients, one with bronchial asthma and the other with myocardial infarction. More detailed descriptions of these studies have been given elsewhere (Westlund and Hougen: *J. Chron. Dis.* 3:34-45 [Jan.] 1956. Life Insurance Companies Institute for Medical Statistics at the Oslo City Hospitals: Myocardial Infarction: An Epidemic and Prognostic Study of Patients from Five Departments of Internal Medicine in Oslo 1935-1949, *Acta med.. scandinav.*, supp. 315, 1956). The expected number of deaths from cancer has been calculated in the same way as for the group with paralysis agitans. The table gives the results in a condensed form. For comparison, data for the patients with paralysis agitans have also been included. It will be seen from the table that actual cancer deaths in the myocardial infarction group were slightly fewer than expected. On the whole, however, the discrepancies between actual and expected deaths in the table are small. A more detailed account of the study, mimeographed in Norwegian, is available on request.

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*Deaths from Cancer, Actual Number and Expected, in Follow-Up Studies for Three Groups of Patients**

					No. of Deaths After Discharge			
					Actual			
		No. of Patients						
Disease	Calendar Yr. of Discharge	Discharged	Not Traced	No. of Observation Yr.	All Deaths	Unknown Cause of Death	Deaths from Cancer	Expected Deaths from Cancer†
Paralysis agitans and Parkinsonism	1917-1950	146	4	763.5	111	3	7	3.6
Bronchial asthma	1917-1936	345	18	5,242.5	183	10	13	11.9
Myocardial infarction	1935-1949	929	0	4,255.5	621	10	17	23.3

* The cause of death is taken from the death certificates.

† Expected number of deaths from cancer is calculated on the basis of the Norwegian cancer mortality rates with regard to age and calendar year distribution.

PSYCHOANALYSIS

To the Editor:—There are some exceptions to be taken to the claims of Freudian psychoanalysis set forth with such conviction in the guest editorial of the July 21 issue of The Journal, page 1160. In reading it one could be led to think that there had not been found anything like vital flaws in its doctrine and that the doctrine had not become much of a controversial issue in psychiatry in general. One need but observe what criticism the doctrine received directly and by implication in some of the papers read at the annual meeting of the American Psychiatric Association this year to become aware of the continuously smouldering conflict that the doctrine's influence in the psychiatric field has provoked and to see that the issue presented is not one to be resolved just by more and more experience and research, but by philosophically reconsidering the principles that are implicated. Some of the papers received rather widespread publicity and served, no doubt, to help keep alive in the popular mind its scepticism about a psychiatry whose doctrinal disunity seems to be so anomalous as it faces the ever-growing incidence of mental disorder in the community. The animus with which this disunity was expressed at that meeting has lead the president of the association to publish in its journal a plea for the adoption of a more tolerant spirit in the treatment of the issue.

The editorial asks for conclusive recognition of psychoanalysis as a scientific discipline. It notes the credit due to Freud for his "discovery of unconscious mental processes." While this unconscious area of the psyche may be seen as part of the evolutional background of man's subjective life, investigation of which therefore involves us at once with the kind of problems that the genetic modality of vital phenomena presents, the editorial seems to overlook its opportunity to claim that Freud had achieved a correct formulation of the genetic process. The key idea of the Freudian doctrine is the genetic idea, and the validity of its claim to being scientific must depend upon the nature of the idea it has adopted.

Freud astutely recognized that the nuclear aspect of so-called functional psychopathology is genetic in its character. He also saw that perhaps the greatest possibility of understanding the basic relationship between organic and psychic phenomena would be seen to exist in a view of the genetic factors that are common to both classes of phenomena. Here he was in agreement with the teachings of Dr. Karl G. Carus who, in Germany in 1831, was expounding the psychic unconscious and the genetic method of understanding it. In principle Freud was also in accord with the theory of degeneration that, in the latter part of the 19th century, was seen by psychiatrists to explain much pathology. But if Freud has achieved a correct formulation of the genetic process in the psychic field, his fame should pervade every sphere of biology, since the process must be identical in nature with that occurring in organic form. Up to now the ontogenetic process has been recognized as the primary and central problem of that science. The application of the Freudian formula to the organic domain should be the test of its validity. The disciple Ferenczi essayed to do some of this with his "bioanalysis." This was consistent, as Freud's formula is mechanistic, paradoxically. It conceives the genetic process as reversible, in spite of the biological impossibilities that this implies. It confuses decomposition with degeneration and involution. Thus the crucial Freudian idea of regression (and restitution) is supported, and it is adhered to although no material tissue changes are found in a patient to correspond to such a process. But the concept of such play of a genetic process, as a principle of pathology, is not used in somatic medicine, and its continued employment in psychiatry must tend to estrange this specialty from the general medical field until the differences are resolved.

No specialty in medicine as much as psychiatry seems to call for an acquaintance with general philosophical principles as basic preparation for research, teaching, and practice. This fact naturally would be recognized distinctly by any doctrine that claims to give anything like a systematic interpretation of psychopathology. But the philosophical position as well as the scientific status of psychoanalysis is ambiguous. It fails to perceive differences in modalities, as when it assumes that the genetic and the mechanistic are interchangeable. It professes to be, in its nature, a science of individuality, since psychiatry perhaps more than any other medical discipline must treat its patient as an individual rather than as a type. But, strictly speaking, science does not know individuals, and this is as true now as when Aristotle said: *"Scientia est de universalibus."* Furthermore, psychoanalysis claims to be scientific in a field where the strictly scientific method again does not apply exhaustively, when it asserts that it has its foundation in biological processes that, in fact, are not understood by biologists or that show no changes of a character that correlate with Freudian mechanisms.

It is necessary to conclude, therefore, that, far from being a basic science, psychoanalysis is itself much in need of whatever reformulation it can undergo that may give it an authentic biological basis. The urgent need of a comprehensive working theory of psychopathology to use in managing the current burden of mental disorder in modern life should not seem to be justification for disregarding this conclusion.

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EDUCATION AND NEUROLOGY

To the Editor:—I have just read Dr. Benjamin Boshes interesting article, "The Responsibility of the Graduate Educator in Neurology and Psychiatry" (*J. A. M. A.* 161:1213 [July 28] 1956), and I anticipate that this will not be the only comment on that somewhat hypercritical paper. Dr. Boshes is an experienced neurologist, but I am certain that his experiences with neurological surgeons cannot have all been as bad as his comments would indicate. While I would not deny that in some of the cases he mentioned there was apparently insufficient justification for heroic diagnostic procedures, I should like to assure him that most neurosurgeons have heard of multiple sclerosis and tension headaches. Indeed we spend much of our time discouraging further neurological examinations for the latter, but in some atypical cases we feel that spinal air studies are the more conservative approach. Most of us can readily recall patients who were given "functional" or "degenerative" diagnoses elsewhere only to have such things as platybasia, intramedullary cervical cord tumor, central cervical disks without plain x-ray changes, or midline cerebellar tumors show up on more thorough study. These are not figments of my imagination but actual examples of cases that had been missed by neurologists, some at famous clinics, who had placed too much reliance on the clinical neurological examination. After all, the most important use of air studies and myelography, etc., is to elucidate surgical lesions where the clinical examination will only allow us to be suspicious of such. Who has not seen a chronic subdural hematoma masquerade as a cerebral thrombosis? Dr. Boshes criticizes an unnamed neurosurgeon for an extremely brief hospital record of his history and physical examination, consisting of the following statements: "Intractable headache, no neurological findings. Impression: Intracranial pathology, tumor? Ventriculography." Dr. Boshes states about the neurosurgeon: "he is mechanically oriented, not broadly grounded neurologically." He makes these assertions in such a way as to give the impression of describing a typical neurological surgeon. I wonder what Dr. Boshes thinks we study during our five plus years of specialty training? Oh, yes, where does one find a hospital these days that permits those brief histories and physicals?

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ROTATING INTERNSHIPS

To the Editor:—In the Aug. 25, 1956, issue of The Journal, page 1664, I have read with concern the resolution passed by the House of Delegates of the American Medical Association to the effect that the Council on Medical Education and Hospitals be requested to increase its efforts to encourage rotating internships rather than straight internships in all hospitals approved for the latter. If this resolution is followed to its logical conclusion, as a condition for approval straight internships will eventually be abolished in favor of rotating internships. Irrespective of the virtues or faults of either type of internship, there appear to me to be three strong objections to such action. 1. The effort to establish rotating internships universally, presumably of two years' duration, would suggest concern not with the improvement of the quality of internship training but rather with the quantity of interns available for hospital appointments. Such a motivation cannot help but result in a deterioration in the quality of internship training. 2. The A. M. A., in its laudable campaign against compulsory health insurance, has repeatedly emphasized the need for preserving our American free enterprise system. Time and again it has demonstrated the dangers to individual liberty that lie ahead if we permit our free institutions to lose even a fraction of the autonomy that has made it possible for them to achieve greatness. The eventual establishment of a uniform rotating internship would restrict the freedom of action of our free and independent hospitals. 3. An institution, one of whose primary functions and objectives is medical education, cannot help but deeply resent the possible imposition of restrictions in the field of medical education. Certainly our large teaching centers have a responsibility to experiment in educational techniques. I believe that most of us in the field of providing hospital and medical care recognize the fine job the Council on Medical Education and Hospitals is doing in its efforts to improve the quality of training available to recent medical school graduates. I hope that it will continue to use its influence for the academic freedom of those individuals in large teaching hospitals who are dedicated to the provision of optimal training for young doctors.

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MISCELLANY

NATIONAL DISEASE AND THERAPEUTIC INDEX

The National Disease and Therapeutic Index, a medical statistical research program, has completed its first few months of operation with the promise of interesting and useful results. Designed to provide information on the nature, scope, and frequency of occurrence of nonfatal disease, injury, and other conditions as seen by the doctor in private practice in the United States, the program involves the compilation of statistical data showing why patients see doctors and what types of treatment they receive. Nearly 800 doctors, located in 27 statistically selected, representative areas in 21 states and the District of Columbia, already are participating in this important project, which has aroused the professional interest of medical men and particularly of medical educators and those involved in both basic and applied research. A recent analysis of the nearly completed national panel showed the following representation by types of practice: 346 general practitioners; 50 obstetrician-gynecologists; 4 obstetricians; 2 gynecologists; 86 surgeons; 110 internists; 50 pediatricians; 17 eye, ear, nose, and throat specialists; 14 urologists; 15 dermatologists; 3 allergists; 21 otolaryngologists; 2 neurosurgeons; and 4 proctologists.

Established to meet the long-recognized need for statistics on morbidity as contrasted with those on mortality, the program was explored thoroughly by members of the American Medical Association staff; representatives of many state, county, and local medical societies; a number of medical educators; and others in the medical profession and allied fields before being put into operation. The nonexistence of reliable data in this area of research and the potential value of such data in both general and specialized medical practice, in research, and in education has been recognized consistently by those consulted.

To accomplish the objectives of the program, a panel of some 864 randomly selected doctors is being established, consisting of approximately 32 men in each statistically selected sample area. The design of the distribution provides for the inclusion of both urban and rural doctors and proper proportional representation of general practice and the various specialties. Each cooperating doctor will report four times per year, giving the age, sex, diagnosis or diagnoses, and treatment used for each patient seen during the course of a 48-hour period once each quarter. In a pilot study conducted with 50 doctors in the Philadelphia area in September, 1955, it was determined that the program was completely feasible and that the required case record for each patient could be completed in less than one minute. Of particular importance to the members of the medical profession and the public is the fact that the names of patients are not involved and the names of reporting doctors are never identified with case records.

To serve as liaison with the reporting doctors and to supervise the operation of the program in each area, 27 coordinators have been appointed. Their function is to assist in enlistment work and scheduling of reporting dates and to do preliminary coding of diagnoses according to the Manual of International Statistical Classification of Diseases, Injuries, and Causes of Death.[1] The reporting doctors are encouraged to use the terminology of the Standard Nomenclature of Diseases and Operations in recording their diagnoses. The coordinators are drawn from among trained medical personnel in each sample area.

The full research facilities of Taylor, Harkins and Lea, Inc., Philadelphia, have been utilized in the organization, development, and operation of the National Disease and Therapeutic Index, and the program has the support of leading ethical pharmaceutical houses. Liaison has been established with the Bureau of Economic Research of the American Medical Association to assure that that organization will be prepared to receive and utilize such data as may, after careful analysis and evaluation, be available. Other organized medical groups and the nation's medical schools should eventually benefit from such useful data as may be developed from time to time as a result of the program.

In summary, the data to be gathered by means of the National Disease and Therapeutic Index eventually should aid medical educators in planning new and revising current curriculums; medical investigators in determining the directions to be taken and the goals to be sought in research; practicing doctors, particularly in their efforts directed toward preventive medicine; health organizations in planning establishment and development of future programs and revision or possible abandonment of current ones; and pharmaceutical manufacturers in research and product development designed to meet current and future needs. Because of the vast scope of the program, it will be some time in the latter part of 1957 before data can be processed and evaluated to determine what may be of benefit to various segments of the profession.

References

1. Manual of International Statistical Classification of Diseases, Injuries, and Causes of Death: Sixth Revision of International Lists of Diseases and Causes of Death, Adopted 1948, Geneva, Switzerland, World Health Organization, 1948.

MEDICAL FILM REVIEWS

Coronary Artery Disease: 16 mm., color, sound, showing time 30 minutes. Prepared in 1956 by and procurable on loan from Claude S. Beck, M.D., 2065 Adelbert Rd., Cleveland 6.

This film begins with a discussion of the cause of death in cardiac ischemia and a method of prevention of death that is effective in 90% of these patients. The film also includes a presentation of animal experimentation work; an autopsy specimen demonstration; a description of the operative procedure used on patients, with a discussion of the reasons for the successful results obtained; and a presentation of 10 patients at various periods from one month to three years after operation. The animal experiments presented include the production of anoxia throughout the entire heart as contrasted with that produced in a localized area through ligation of a primary coronary vessel. The latter condition sets up a trigger-like mechanism that may produce cardiac fibrillation and death. The Beck operation, which results in the prevention of death in 90% of patients with cardiac ischemia, is described as follows: (1) mobilization of and placing a ligature around the coronary sinus; (2) abrasion of the pericardium and epicardium; (3) ligation of the coronary sinus on a 3-mm. probe, to maintain that amount of lumen for return flow of venous blood to the right side of the heart; (4) the placing of 0.2 gm. of ground asbestos on the epicardium to stimulate the production of vascular adhesions; and (5) the suturing of both pericardium and pericardial fat to the heart. In dogs in which this procedure is done the heart is protected to the extent that the mortality rate is only 26% after the ligation of the descending ramus of the coronary artery, as compared to a mortality rate of 70% when this procedure is not carried out. The back-flow test of coronary circulation is increased more than 5% after the operation is performed, giving rise to as much as 282 cc. of blood flow per hour in these experiments. Through improvement of communications between coronary arteries, the myocardium is preserved in a better condition. Just prior to the time this film was made, the mortality rate in 100 human beings on whom this type of operation had been performed was 6%. Of the 10 patients presented in this film, 9 are working, and all are either completely relieved or markedly improved since operation. Some mention should be made, in the film, regarding the selection of patients and the indications for and contraindications to the operation.

Dr. Beck introduces the film in person and narrates it well. Color is excellent, and the exposure is adequate at all times. Since this film includes much scientific data as well as operative technique, it would be useful in teaching, especially at the graduate level. It would be of special value for graduate teaching in cardiac surgery.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Treatment of Carbon Monoxide Intoxication by Cytochrome. J. F. Gros and P. Leandri. Presse méd. 64:1356-1357 (July 28) 1956 (In French) [Paris, France].

Carbon monoxide injures the cytochrome system. Cytochrome treatment in carbon monoxide intoxication is therefore of great importance. Its therapeutic effects vary according to the previous condition of the victim, the time of exposure in a toxic atmosphere, and the degree of carbon monoxide concentration. Clinical material is scarce, and further cases must be reported before a definite conclusion can be reached. So far, 20 patients in coma due to carbon monoxide intoxication have been treated by cytochrome medication after having been given the usual artificial respiration and inhalation of oxygen. Blood-letting and injections of novocaine and of cardiorespiratory analeptics were also used. Cytochrome was given by intravenous injection, in doses of from 15 to 60 mg. of cytochrome C in isotonic sodium chloride solution; the maximum dose at one injection was 30 mg., repeated 15 minutes later when necessary. All the patients revived in from 8 to 30 minutes after administration of the drug, and all survived except two who died later as a result of secondary complications. There were no side-effects except for vomiting in one case. The duration of the coma seems to be shortened by cytochrome treatment; cardiopulmonary conditions improve; and cyanosis disappears quickly.

Survival Rates After Acute Myocardial Infarction with Long-Term Anticoagulant Therapy. J. W. Keyes, E. H. Drake and F. J. Smith. Circulation 14:254-259 (Aug.) 1956 [New York].

Continuous long-term anticoagulant therapy with bishydroxycoumarin (Dicumarol) was practiced at the cardiology division of the Henry Ford Hospital, Detroit, in 121 selected patients with acute myocardial infarction. A group of 234 unselected patients with acute myocardial infarction who had been treated at the same hospital before the use of anticoagulant drugs for this condition and who received the same general medical care as the 121 selected patients served as controls. Both groups were divided into two subgroups, one consisting of patients with a single infarct and one in which the patients had survived the acute phase of two or more well-substantiated episodes of acute myocardial infarction before being placed on therapy. A comparison was made of the death rates of the treated and the control groups with mortality determinations made at six-month intervals for the first two years and then at yearly intervals up to five years. The rate of death in the group with single infarct was three times greater for patients not receiving anticoagulants. In the group with recurrent infarcts the rate of death was five times greater without anticoagulant therapy than with it. Seven new myocardial infarctions occurred among the 121 patients receiving anticoagulant therapy, an incidence of 5.7% The prothrombin time was determined with the Quick two-stage method and was considered adequate in five, unsatisfactory in one, and unknown in one of the seven patients. Twelve deaths (9%) occurred among the 121 treated patients as compared with 112 (48%) among the 234 control patients. Hemorrhage was a contributing cause of death in three of the seven patients in the treated group, although in none was death caused by blood loss alone. Anticoagulant therapy was discontinued in 28 patients who had been started on a long-term program; in 14 patients therapy was discontinued because of hemorrhage, and the other 14 patients discontinued treatment of their own accord. New infarcts occurred in 14 of the 28 patients during a period of from 3 day to 20 months after withdrawal of the anticoagulants. Thus the incidence of acute myocardial infarction among patients discontinuing therapy is high. Six of these 14 infarcts were fatal. One patient had a popliteal embolus after cessation of anticoagulant therapy, and the remaining 13 patients were alive 4 to 54 months after therapy had been discontinued.

In the course of five years of long-term anticoagulant therapy, bleeding occurred 54 times in 51 patients (42.1%). "Serious" or "major" bleeding occurred in 16 patients (13.2%) and minor bleeding in 35 (29%). In view of the time involved, the incidence is not excessive, since the hazard from hemorrhage is considerably less than that from the progress of the disease. Hemorrhagic manifestations do not constitute a contraindication to anticoagulant therapy. A trained anticoagulant team, working with a well-equipped laboratory, is necessary for the success of anticoagulant therapy. Regular weekly prothrombin determinations must be made. Long-term anticoagulant therapy has been particularly effective in patients with recurrent infarcts.

Local Treatment of Arthropathies with High Doses of Hydrocortisone Acetate. Reumatismo 8:214-219 (July-Aug.) 1956 (In Italian) [Milan, Italy].

Fifty-six patients with rheumatic and articular disease were treated with intra-articular injections of hydrocortisone acetate. The doses were considerably higher than usual. In 20 patients with rheumatic arthritis the drug was almost always injected into the knee; the patients were followed for at least one month; results were very good in 17 cases and good in 3. Twenty-seven patients had arthrosis; negative results followed in only two cases. Injections of 5 cc. of hydrocortisone, equivalent to 125 mg. of hydrocortisone acetate, were always well tolerated. The qualitative effect of high doses of the drug is similar to that of low doses of the drug, but the quantitative effects are much better. Results last longer and repetition of the treatment can be avoided. Longer-lasting results were obtained in patients with rheumatic arthritis who were also undergoing treatment with prednisone. Five cases of periarthritis were cured rapidly with one injection, and the results were still good after a month.

The Prevention and Correction of Deformity in Rheumatoid Arthritis. N. Swanson. Canad. M. A. J. 75:257-261 (Aug. 15) 1956 [Toronto, Canada].

Both knees, both elbows, and many finger joints of a 16-year-old boy were painfully swollen due to rheumatoid arthritis. They were immobilized in plaster-of-Paris splints, which prevented all painful movements and so relieved the muscle spasm. The temperature and erythrocyte sedimentation rate fell toward normal, and body weight later rose rapidly. Joint immobilization marked the turning point in the illness and in some way also favorably affected the systemic manifestations. Muscle spasm is the initiating cause of deformity in rheumatoid arthritis. If a splint can act as an artificial spasm-substitute, the physiological spasm, whose fundamental purpose is to fix the joint in slight flexion in order to prevent movement that worsens the pain caused by the inflammatory process, will no longer be necessary and the muscle will relax. In the case of a 65-year-old man, a posterior, nonpadded skin-tight splint of plaster-of-paris was applied to the leg. The left knee was in 45-degree flexion when the splint was applied. At the end of seven days the cuffs were removed. The ankle was lifted up with the thigh remaining inside. For several days afterward, the leg was lifted out for exercise only and then replaced in the splint with a bandage instead of the cuffs to restore the immobile state. The exercises

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The place of publication of the periodicals appears in brackets preceding each abstract.

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included gentle flexion a few times only each day. After another four days a fresh splint was made with the same technique, with the leg in the new position in order to consolidate the gain made. The leg was nearly straight when the second cast was removed after an additional week.

Not only knee joints but also hand deformities lend themselves to correction readily by correctly applied light splints. Two cases, one of a 51-year-old man and one of a middle-aged woman, illustrate the improvement which took place in their hands, with increased range of flexion and extension of the fingers obtained by wearing light, comfortable splints continuously at first and later intermittently. Splints are a valuable and often essential part of the treatment of rheumatoid arthritis, especially when a joint is acutely and painfully swollen; when muscle spasm about a joint is producing deformity; and when subluxation has impaired function, which could be improved if the extremity or a part of it were held in a better position.

A Clinical and Pathological Study of Sixteen Cases of Rheumatoid Arthritis with Extensive Visceral Involvement ("Rheumatoid Disease"). R. J. G. Sinclair and B. Cruickshank. Quart. J. Med. 25:313-332 (July) 1956 [Oxford, England].

Patients who have arthritis of the rheumatoid type may have involvement of tissues other than the joints. Three types of lesions have been described in previous accounts of systemic involvement: granulomas, nonspecific inflammation, and amyloidosis. This report is concerned with clinical and pathological data on 16 patients with widespread systemic involvement. Thirteen of the patients were women and three were men. The main lesions found were granulomas in the heart (five cases) and elsewhere (two cases), arteritis (nine cases), pleurisy (seven cases), splenomegaly (four cases), lymphadenopathy (four cases), lymphorrhages in muscles and nerves (nine cases), and amyloidosis (four cases). Rheumatoid endocarditis was present in eight patients, with clinical evidence in seven. Some combination of myocarditis, coronary arteritis, or pericarditis was present in another five patients, all of whom showed clinical features of cardiac involvement. Pleurisy had occurred in 12 patients, in 7 of whom no etiological factor could be found. Further evidence is presented to show that unexplained pleurisy is very common in rheumatoid arthritis.

Amyloidosis is regarded as a systemic manifestation of the disease. The visceral lesions of rheumatoid arthritis were the main cause of death in eight patients and a major contributory factor in another seven patients. None of the lesions was considered to be the result of treatment. The term rheumatoid arthritis refers to a nonspecific lesion confined to the joints. It is suggested that cases in which other tissues are involved should be called rheumatoid disease. The authors regard it as unfortunate that rheumatoid disease and arthritis of rheumatoid type have been included under the heading "collagen diseases," for the evidence at present available does not justify this step. All the lesions of rheumatoid disease affect mesodermal or connective tissues, but it is not possible to pick out a common basic change in all the different sites. Although many of the changes are nonspecific, they occur often enough to be regarded as part of the disease. There are differences of opinion about the part played by collagen in the granuloma of rheumatoid disease and about the composition of the fibrinoid material that is one of its main features. It does not seem possible that all the lesions of the disease can be explained on the basis of a primary abnormality of collagen.

The Rash of Rheumatoid Arthritis and Still's Disease. I. C. Isdale and E. G. L. Bywaters. Quart. J. Med. 25:377-387 (July) 1956 [Oxford, England].

Isdale and Bywaters believe that the rash that may occur in rheumatoid arthritis and in Still's disease (multiple rheumatoid arthritis affecting children and marked by enlargement of lymph nodes, particularly of the spleen and by irregular fever), has received insufficient attention. Although it is usually considered infrequent, in the experience of these authors it is not uncommon, and, since it is easily recognizable, it has proved of great diagnostic value, particularly in early cases without arthritis. The authors surveyed 166 cases of Still's disease seen in the Canadian Red Cross Memorial Hospital in the last 7 years and over 500 cases of rheumatoid arthritis seen at the Postgraduate Medical School of London during the last 15 years. In all cases designated as Still's disease the condition had started before the 16th birthday. The diagnosis in all cases was based on the presence or development of polyarthritis of the rheumatoid type affecting a number of joints, or, in juvenile cases where less than four joints were involved, on synovial biopsy showing characteristic rheumatoid changes. The characteristic rash consists of small macular lesions, 3 mm. or less in diameter, with a slightly irregular margin. Larger lesions may sometimes occur and may show central pallor. Less commonly the rash may appear confluent over areas up to 5 cm. in diameter. It may be slightly raised, especially when it first appears, but does not itch. Such papules usually become flattened, but occasionally small ringed areas with slightly raised margins may be seen. The rash is bright salmon-pink in color: it is usually surrounded by a narrow areola of normal skin that is paler than its surroundings. Lesions occur most frequently on the limbs and over the trunk, less often on the face and neck.

This rash occurred in 46 (27.7%) of 166 children with Still's disease. It was also observed in 7 of more than 500 adults with rheumatoid arthritis. The rash is frequently associated with intermittent fever, splenomegaly, lymphadenopathy, and other signs of activity of the disease, particularly a raised sedimentation rate. It is transient, appears towards evening and with high temperatures, and does not spread. It may last, on and off, for a week or for many years. It appears usually within two weeks of the onset of the disease or may precede other manifestations by a period ranging from six months to three years. Histologically it is characterized by a sparse infiltrate of polymorphonuclear cells in the subepithelial layer. The effects of various local procedures were tried on the rash. The application of hydrocortisone ointment twice daily was ineffective. Intracutaneous injection of isotonic solution of sodium chloride was likewise ineffective, but local injection of hyaluronidase inhibited the formation of the macules.

ABO Blood Groups and Gastro-Duodenal Diseases. B. P. Billington. Australasian Ann. Med. 5:141-148 (May) 1956 [Sydney, Australia].

The investigations reported here were undertaken to ascertain whether the associations of gastroduodenal diseases and ABO blood groups were as valid for Australia as for the United Kingdom. Records of public inpatients at a Sydney hospital were analyzed during the period 1947 to 1954. As blood grouping is not performed on all inpatients, only those cases in which data were available by virtue of transfusion for bleeding or surgical intervention could be admitted to this series. No immigrants were included. The author was able to adduce evidence that there is an association between chronic duodenal ulcer and blood group O, but no significant difference in the ABO blood group distribution was found between controls and patients with chronic gastric ulcer taken as a whole. Patients with chronic gastric ulcer may be divided into two significantly different populations with regard to ABO blood group distribution according to the site of the ulcer. To a degree differing significantly from that found in a control population, prepyloric ulcer appears to be associated with blood group A and nonprepyloric ulcer with group O. Carcinoma of the stomach in this small series was not found to be associated with blood group A, as had been observed in Britain. Patients with carcinoma of the stomach can also be divided into two significantly different populations with regard to ABO blood group distribution according to the site of origin of the neoplasm. To a degree differing significantly from that found in a control population, prepyloric carcinoma appears to be associated with blood group A and nonprepyloric carcinoma with blood group O. The association between carcinoma of the stomach and blood group A found in Britain may be explained by a higher proportion of prepyloric carcinoma there than in the present series.

Association between chronic gastric ulcer and gastric carcinoma and the ABO blood groups appears to be governed in part by the site of lesion, prepyloric lesions being associated with blood group A and nonprepyloric lesions with blood group O, irrespective of the nature of the lesion. There is no explanation for the association between ABO blood groups and gastroduodenal disease. It seems possible that gastric mucous secretions may be more important than gastric parietal (acid) secretions in such associations. If ABO blood groups are associated with gastric resistance or susceptibility factors, and if a relationship to a single gene is involved, then it would appear from this small series that an association with blood group gene O is more likely to be implicated with protection of the prepyloric mucosa to both ulcerogenic and carcinogenic factors.

Chronic Cough: Analysis of Etiologic Factors in a Survey of 1,274 Men. A. M. Phillips, R. W. Phillips and J. L. Thompson. Ann. Int. Med. 45:216-231 (Aug.) 1956 [Lancaster, Pa.].

A study of 1,274 men was carried out in an attempt to determine the incidence of chronic cough. For analytical purposes, the men studied were divided into two groups between which there were geographical, residential, and occupational differences. Group 1 was composed of 974 men employed in a large steel-making plant in West Virginia, and group 2 consisted of 300 male patients chosen at random from the medical and surgical wards of the Veterans Administration hospital in Providence, R. I. The men in group 1 worked in and most of them resided in or near a single, highly industrialized urban community in which the general air environment contained considerable dust and smoke. Two hundred ninety-seven (31%) of the 974 men had chronic cough. The 300 in group 2, from which patients with specific pulmonary disease, congestive heart failure, and advanced terminal disease were excluded, lived in scattered areas of New England, including rural and urban communities with none or only mild air pollution. One hundred thirty-two (44%) of the 300 men had chronic cough. Thus 429 (34%) of the total of 1,274 men gave a history of chronic daily cough with sputum. The findings failed to show that residence in a generally more polluted urban atmosphere leads to increased incidence of chronic cough.

In addition to the general environmental factors, those of previous pulmonary infection, smoking habits, and age were evaluated. Correlation was found between cigarette smoking and chronic cough. This was shown by the direct effect of the quantity of cigarettes smoked daily, the cessation of cough in the men who stopped smoking, and the striking increase in cough with age in the smokers. No direct correlation was seen with any of the other factors except age, and this was of importance chiefly in those who smoked cigarettes. It is suggested that, in view of these findings, certain factors such as industrial exposure, commonly considered as important in causing chronic cough and bronchitis, may need reevaluation. Comparison between smokers and nonsmokers would seem to be an integral part of such studies. The high incidence of chronic cough in the older age group of cigarette smokers, together with its duration, may well be related to structural changes in the lungs of such persons. The development of chronic bronchitis secondary to inhalation of cigarette smoke deserves consideration as the most common cause of pulmonary emphysema.

A New Intra-Arterial Treatment of Arterial Diseases of the Lower Extremities. P. Šnábl, Z. Fiala and F. Polak. Ztschr. ges. inn. Med. 11:660-665 (July 15) 1956 (In German) [Leipzig, Germany].

The intra-arterial administration of drugs in the treatment of arteriosclerotic disorders has the advantage of producing, even with the administration of relatively small doses, a comparatively high concentration at the site of action. The authors report their experiences with the following: (1) procaine hydrochloride in a dose of 10 ml. of a 1% solution; (2) nicotinic acid with ethanol amine (Neopeviton) in a dose of 5 or 10 ml.; (3) heparin in a dose of 5,000 anticoagulation units; and (4) tetraethylammonium bromide (TEAB) in a dose of 3 to 10 ml. The drugs were given daily by injection into the femoral artery. A course of treatment consisted of either 15 to 20 or 20 to 30 injections. Each drug was studied in six patients and its evaluation was based on the claudication test and on the temperature and color of the skin. The number of steps the patient was able to take before and after treatment during the claudication test provided a quantitative indicator for the therapeutic effect and could be statistically evaluated. The other criteria were suitable only for qualitative analysis. All the data indicated that tetraethylammonium bromide was much more effective than the control drug procaine hydrochloride, and the other drugs had usually about the same effect as procaine hydrochloride. Since the injections of tetraethylammonium bromide into the femoral artery were well tolerated and since, unlike intravenous injection, intra-arterial injection of this drug did not reduce the blood pressure excessively, the authors feel that the intrafemoral administration of tetraethylammonium bromide can be recommended for the treatment of obliterative disorders of the lower extremity.

Indications for Hydrocortisone and Prednisone Treatment of Progressive Pulmonary Tuberculosis: Four Years' Experience with 70 patients. G. Favez and F. Aguet. Schweiz. med. Wchnschr. 86:843-851 (July 28) 1956 (In French) [Basel, Switzerland].

Extensive progressive pulmonary tuberculosis with predominantly pneumonic foci, recent in appearance, and acute miliary tuberculosis call for treatment with hydrocortisone and prednisone in combination with antibiotics. Prednisone gives better results. Resorption of the parenchymal opacities is remarkable, and so is the steady improvement in general health. Corticotherapy, which is only an initial treatment, should be followed by continual antibiotic and bacteriostatic therapy. However, the therapeutic effects of adrenal hormones are not sufficiently well known, and the side-effects are not so slight as to justify inclusion of cortisone medication in the usual therapeutic pattern in tuberculosis. Tuberculous meningitis constitutes another indication for cortisone therapy. A careful study of the patient and the efficient prophylaxis provided by antibiotics make possible the employment of similar preparations in acute cases.

Twenty patients with pneumonic tuberculosis with extensive onset were improved clinically and radiologically during treatment with hormones. Many of them would have died without the help of cortisone therapy. The first to be treated, who were the most seriously affected, have been able to return to their work. Two years have elapsed and symptoms have not reappeared.

Acute Gastritis as the Cause of Otherwise Unexplained Upper Gastrointestinal Hemorrhage. E. L. Posey Jr. and S. L. Stephenson Jr. Am. J. Gastroenterol. 26:137-149 (Aug.) 1956 [New York].

Acute gastritis is a not infrequent cause of gastrointestinal

The behavior of acute gastritis with hemorrhage differs completely from that of chronic gastritis. The exogenous agent, be it alcohol or an allergen, apparently produces a sudden violent mucosal reaction with congestion, erosion, and hemorrhage, which heals without residual symptoms in a few days' time. None of these patients died, and not a single case of fatal hemorrhage from gastritis has been found in the literature. Apparently this condition is essentially a benign disorder, even though the blood loss may be severe.

Clinical Experience with Streptomycin of "Reduced Toxicity" (Streptothenat) in Treatment of Tuberculosis. G. Jaccard and T. Becht. Schweiz. med. Wchnschr. 30:862-864 (July 28) 1956 (In German) [Basel, Switzerland].

Forty-one patients with pulmonary tuberculosis, three with tuberculous pleurisy, and two with tuberculous meningitis were given intramuscular injections of streptothenat, a mixture of 80% of streptomycin sulfate and 20% of streptomycin pantothenat. Most of the patients were given injections of 1.5 or 2 gm. of streptothenat two or three times a week; they had no local pain, and only 10 patients had dizziness or headache. Thirteen patients who were given 3 or 4 gm. of the drug twice a week had toxic side-effects consisting of damage to the vestibular nerve.

Streptothenat was given a trial in this small number of patients in an attempt to determine whether this compound, which exerts the same tuberculostatic effect as streptomycin, can be given in higher doses than streptomycin sulfate without causing undesirable side-effects. The clinical experiences in the 46 patients and determinations of the concentration of streptothenat in the blood of 11 of these patients suggest that strepothenat can be given in larger doses than streptomycin sulfate, provided that intermittent treatment with doses of 1.5 or 2 gm. two or three times a week is practiced for three months. Because of the general tendency to give tuberculostatic therapy for one year or longer, one should at present continue the streptothenat therapy after three months with smaller doses until additional experience has been gained. The number of patients is too small and the follow-up period too short to evaluate the therapeutic effect of the doses employed.

SURGERY

Status of Fifty Patients Four and a Half to Seven Years After Mitral Commissurotomy. O. H. Janton, J. C. Davila and R. P. Glover. Circulation 14:175-184 (Aug.) 1956 [New York].

The authors report a follow-up on the first 50 patients who underwent mitral commissurotomy four and a half to seven years ago. There were 36 women and 14 men. At the time of the intervention the patients were between the ages of 17 and 47 years. Before their admission to the hospital for the operation 20 patients had a rheumatic infection, 23 had hemoptysis, and 27 had one or more attacks of congestive heart failure. On admission, 13 patients had chronic congestive heart failure and 19 had permanent atrial fibrillation. Three patients died in the course of the first postoperative month, representing an operative morality of 6%; death in one who died two hours after the operation was apparently caused by operative and anesthetic shock, one died of acute cardiac failure, and one of excessive mitral insufficiency. Six patients with extensively calcified valves died within a period of from six weeks to three years after commissurotomy, thus representing a late morality of 12%. Irreversible cardiopulmonary, hepatic, and renal disease at the time of the surgical intervention was responsible for the deaths of three of these patients; two patients had inoperable valves that precluded successful commissurotomy, and in one patient preexisting mitral insufficiency was aggravated by the operation.

Thus 41 patients (82%) were living at the time the paper was written, and clinical findings, electrocardiographic tracings, teleroentgenograms, and catheterization data obtained from these patients were evaluated. Only 4 of the 41 patients had no murmurs on follow-up examination; 11 did not have their original mitral diastolic murmur and 14 had mitral systolic murmurs of varying intensity that were not present preoperatively. Definite conclusions regarding the present clinical status of these patients could not be reached from their murmurs alone. Patients with "pure" mitral stenosis obtained the best results from mitral commissurotomy. Although the electrocardiographic changes after surgery did not regularly show conclusive evidence of improvement, there was a small group of patients in whom postoperative regression of right ventricular hypertrophy occurred. Fluoroscopic and teleroentgenographic studies revealed that in 44 patients (87%) the size of the heart was the same as or smaller than before the surgical intervention, whereas in the years preceding the operation the size of the heart had grown progressively larger. The available cardiac catheterization data paralleled and corraborated the observed functional state of the patients. Twenty-one patients (51%) without valvular calcification showed greater improvement than the 20 patients (49%) with valvular calcification. Evidence of rheumatic activity was observed in the course of the postoperative period in eight patients (19.5%). Valvular stenosis was not observed in the 41 living patients nor in those who died during the postoperative period. An embolus occurred in only one patient during the operation, and that patient recovered almost completely. There were no postoperative emboli. Twenty-nine (71% of the living patients or 58% of the original 50 patients) were in better condition and living a more nearly normal life than they were before the operation. Commissurotomy confers a genuine, often dramatic, and usually persistent benefit on the patient.

Congenital Cirsoid Aneurysm of a Coronary Artery with Associated Arterio-Atrial Fistula, Treated by Operation: A Case Report. H. E. Mozen. Ann. Surg. 144:215-217 (Aug.) 1956 [Philadelphia].

A case of congenital cirsoid aneurysm of the left coronary artery associated with an arterioatrial fistula in a 10-year-old boy is described. Except for slight dyspnea on extreme exertion, the child was asymptomatic. The blood pressure varied between 120/80 and 130/60 mm. Hg. The pulse rate was 84 per minute. The size of the heart was normal. A loud, continuous, to-and-fro murmur with systolic accentuation was heard in the pulmonic area. A lower-pitched systolic murmur was also heard at the apex. There was questionable diminution of the peripheral pulmonary vascular markings. Cardiac catheterization was performed and was technically satisfactory. Pressures and oxygen concentrations in the pulmonary artery, right ventricle, right atrium, and venae cavae were normal. When the pericardium was opened, a tremendously dilated and tortuous vessel was found overlying the interventricular septum in the usual location of the anterior descending branch of the left coronary artery. In many places, large branches disappeared abruptly into the myocardium of the left ventricle. One branch, which was 1.5 cm. in length and 0.5 cm. in diameter, appeared to empty directly into the left atrium. Compression of this vessel obliterated the harsh thrill. Evidently this was a fistula that was carrying large amounts of blood from the high-pressure aneurysm into the low-pressure left atrium. The fistula was doubly ligated. The aneurysm immediately became smaller in diameter, and the thrill disappeared completely. The postoperative course was uncomplicated. The murmurs disappeared, and the heart sounds became normal and remained so.

The case described is the 52nd instance of an aneurysm of a coronary artery to be reported. It is the first case in which the diagnosis was made at operation; in the other 51 cases the diagnosis was made at autopsy. This is also the first case in which an associated arterioatrial fistula has been cured by operation. The possibility of making a correct preoperative diagnosis is considered.

Stump Recurrence and Total Thyroidectomy in Papillary Thyroid Cancer. F. F. Rundle and A. G. Basser. Cancer 9:692-697 (July-Aug.) 1956 [Philadelphia].

Stump recurrence in the sense of recurrent carcinoma in the fragment of thyroid gland remaining after incomplete lobectomy must generally be regarded as due to a surgeon's failure. There has been an insufficiently wide extirpation of a growth that is only locally malignant. The authors describe two cases of papillary thyroid cancer with multiple foci in a 34-year-old man and in an 18-year-old girl that illustrate the pathological aspects that have a practical bearing on surgical treatment. Multiple foci are virtually confined to the papillary and to the mixed papillary and follicular growths occurring in young people. These multiple foci may represent seedlings resulting from intraglandular lymphatic spread rather than separate primary foci. The satellite foci may be microscopic in size and separated from the obvious nodule by apparently normal thyroid tissue several centimeters in thickness. The foci may be bilateral as well as small in size. Spread from a tumor in one lobe may occur to the contralateral cervical lymph nodes. The juxtathyroidal nodes, including the pretracheal nodes above and below the thyroid isthmus, those around the thyroid veins, and those in the tracheoesophageal groove, in contrast to the lateral cervical nodes, lie on or near the vital structures of the trachea and the esophagus, and it is therefore highly desirable that they be removed while their invasion is still microscopic in extent. With the lateral cervical nodes, however, a policy of "wait and see" seems permissible.

Potentially the most serious invasion is that occurring medially and posteriorly. Medial extension occurs most commonly to and through the wall of the trachea, between the cartilaginous rings. Thence spread occurs upward and downward in the submucous layer of the trachea, forming an intraluminal growth that heaps up, leading to obstruction, ulceration, and hemorrhage. Spreading posteriorly, papillary growths involve structures in the tracheoesophageal groove, the recurrent nerve, prevertebral muscles, and spinal nerves, and even invade the spinal canal, as happened three and a half years after a "thyroidectomy" in a third patient, a 24-year-old woman. Heavy postoperative irradiation with a dose of 3,500 r led to widespread skin atrophy and dense sclerosis of all the tissues at the root of the neck; it masked, and ultimately precluded excision of, the subsequent stump recurrence. Anything short of complete extrafascial thyroidectomy with resection of the juxtathyroidal nodes may, therefore, be followed by a recurrence at the thyroid site. A plea is made for the general use of frozen sections when operating on suspicious thyroid nodules. The routine use of "prophylactic" deep roentgen-ray therapy after operations for papillary cancer is disadvantageous and should be abandoned.

Congenital Aortic Stenosis: Clinical Aspects and Surgical Treatment. D. F. Downing. Circulation 14:188-199 (Aug.) 1956 [New York].

Twenty-nine male and eight female patients between the ages of 4 months and 39 years with congenital aortic stenosis were studied. Fatigue, shortness of breath, and profuse perspiration were the commonest symptoms. Central nervous system manifestations and chest pain were infrequent. A loud, harsh systolic murmur in the second and third right interspaces near the sternal border was observed in all the patients, and in 19 it was accompanied by a systolic thrill. These physical signs are of great diagnostic significance because they are rarely found in this location in patients with other malformations. On roentgen-ray examination the most frequent manifestation was dilatation of the ascending aorta. Electrocardiographic evidence of left ventricular hypertrophy was found in 22 patients. Catheterization of the right side of the heart was completed in 31 patients, simultaneous catheterization of the left and right sides of the heart was done in one, and in another the right and left sides were catheterized at different times. Catheterization of the right side of the heart proved to be helpful in ruling out other lesions. Catheterization of the left side of the heart was diagnostic in a patient in whom a gradient in systolic pressure across the valve was demonstrated. Differentiation of valvular from infundibular stenosis was not possible.

Relief of severe obstruction is mandatory because of the danger of sudden death. A satisfactory procedure is available for correction of valvular stenosis. It involves the dilatation of the narrowed orifice by an instrument inserted into the left ventricle. This operation was performed on 10 children, 2 of whom were less than 3 years of age, and on 9 adults. There is no optimal age for the surgical intervention; there is only the age of opportunity. There was one operative death, which resulted from irreversible cardiac failure in a 36-year-old man; in addition, an 18-year-old patient died eight months after the operation. One patient with infundibular stenosis was a therapeutic failure. In the remaining 16 patients there was objective evidence of improved flow across the aortic valve. Symptoms were improved in 14 patients, one had had no symptoms preoperatively but had been in cardiac failure in early life, and symptoms became worse in one patient who did not receive proper postoperative care. Although it is too early to judge the results, all but two of the surviving patients appear to have been helped.

Congenital Intrinsic Duodenal Obstruction: Report of 32 Cases. T. C. Moore. Ann. Surg. 144:159-164 (Aug.) 1956 [Philadelphia].

A statistical review is presented of 32 cases of congenital intrinsic duodenal obstruction in 17 baby boys and 15 baby girls (30 white and 2 Negro), 21 of whom were operated on at the department of surgery of the Indiana University Medical Center between 1942 and 1956. Symptoms of complete obstruction from birth were observed in all infants with atresia and in one-half of those with stenosis. Atresia was found more frequently in proximal duodenal obstruction, whereas a distal lesion was more likely to be a stenosis. A plain roentgenogram of the abdomen is regarded as the most reliable single diagnostic measure. Eight (25%) of the 32 infants were premature. Additional congenital malformations were discovered in 13 infants (41%). Duodenojejunostomy was performed in 15 patients, gastrojejunostomy in 5, and duodenoduodenostomy in one. Eighteen (86%) of the 21 infants operated on recovered and 3 (14%) died. Two of the three who died were premature and had additional congenital anomalies.

Bronchogenic Carcinoma with in Situ Carcinoma in the Opposite Lung: Report of Five Cases. R. F. Ryan and J. R. McDonald. Proc. Staff Meet. Mayo Clin. 31:478-485 (Aug. 22) 1956 [Rochester, Minn.].

Ryan and McDonald studied autopsy specimens from 39 men from whom one lung had previously been removed for squamous-cell carcinoma. In all cases the bronchial epithelium of the remaining lung appeared normal on gross examination. Yet when sections were taken from these "good" lungs and examined microscopically, extensive changes in the bronchial epithelium were found. In five cases definite areas of in situ carcinoma of the squamous-cell variety were found. The authors believe that these lesions represent new foci of malignant degeneration and not metastatic disease. While these changes were more pronounced in the main-stem bronchi, similar changes were also found in the tertiary bronchi, as demonstrated in one of the five cases. It is difficult to know how significant these in situ lesions in the opposite lung may be, but it can be assumed that some patients who obtain poor results from operation actually may have new lesions rather than extension, recurrence, or metastasis from the primary lesion. Since the contralateral in situ lesions are multicentric and may have a long latent period, the finding of an in situ lesion at the coryna on bronchoscopic biopsy might not be a valid contraindication to operation if the primary lesion is otherwise operable.

GYNECOLOGY & OBSTETRICS

Defective Blood Coagulation Associated with Intrauterine Foetal Death. J. M. Farrar. M. J. Australia 2:65-68 (July 14) 1956 [Sydney, Australia].

Moderate or severe concealed accidental hemorrhage, long-standing intrauterine fetal death, amniotic fluid embolism, and tumultuous labor are possible precursors of a clotting defect. The coagulation defect in the above conditions may be due to various abnormalities, but the most important are diminution in amount or absence of the blood fibrinogen (hypofibrinogenemia or afibrinogenemia) or the presence of an active fibrinolysin. Hypofibrinogenemia and fibrinolysis may occur separately or together. Hypofibrinogenemia in most instances is probably due to excessive utilization of the circulating fibrinogen or to its destruction by fibrinolysin. Excessive utilization of fibrinogen may occur in the presence of severe hemorrhage associated with fibrinolysis because the clots are immediately dissolved. Fibrinogen levels in the blood may be low in the absence of hemorrhage when the circulation is flooded with material rich in thromboplastin (liquor amnii or products of placental degeneration or damage), because coagulation is initiated and a film of fibrin is deposited on the vascular endothelium. The total quantity of circulating fibrinogen in the body amounts to from 8 to 12 gm., and a 500-cc. blood transfusion may increase the level of fibrinogen by 10 to 20 mg. per 100 cc. The liver can replace the lost fibrinogen rapidly, and in the less severe cases the fibrinogen may be kept above the critical level by regeneration with or without blood transfusion. This may be impossible in the more severe cases, and it is in them that the intravenous administration of fibrinogen may be life-saving.

Intrauterine fetal death assumes a new importance now that it is recognized that it may be associated with impaired coagulation of the blood. The author presents the history of a woman in whom a coagulation defect was associated with longstanding retention of a dead fetus in utero. During her first pregnancy (in 1949) she had had a miscarriage at three months. The second and third pregnancies in 1950 and 1952, respectively, ended with the delivery at term of a macerated fetus that had been dead for one month. No maternal anti-Rh agglutinins were detected. In the present pregnancy fetal movements ceased during the 23rd week. Labor was induced by a drip administration of pitocin after intrauterine retention of a dead fetus for 11 weeks. Contractions had been present for three hours when it was found that blood escaping from the vagina did not clot. When blood was collected for testing an unstable clot formed, which redissolved in 15 minutes. An increased rate of blood loss followed the expulsion of the fetus one and a half hours after the initial hemorrhage. The total blood loss was estimated at two liters. Two and a half liters of blood (containing an estimated 4.5 gm. of fibrinogen) and 4 gm. of fibrinogen were given. The patient was discharged from the hospital on the seventh day.

Vulvovaginitis as Complication in Antibiotic Therapy. K. Bjøro. Tidsskr. norske lægefor. 76:479-480 (July 1) 1956 (In Norwegian) [Oslo, Norway].

A case of postpartum vaginal moniliasis with severe exacerbation during and after treatment with Aureomycin is reported. The patient's husband was also infected with moniliasis. Local treatment with Nystatin, an antibiotic derived from Streptomyces noursei, proved effective. Candida albicans is frequently part of the normal vaginal flora, most often in pregnancy and directly after delivery, and the danger of promoting its growth by the use of antibiotics, especially those of the tetracycline group, is emphasized.

Congenital Adrenal Hyperplasia (Pseudohermaphroditism) Before and After Cortisone Therapy: I. Adolescent Development and Menstruation. E. K. Smith and R. R. de Alvarez. Am. J. Obst. & Gynec. 72:404-415 (Aug.) 1956 [St. Louis].

A case of congenital adrenal hyperplasia is described in a 16-year-old girl with the chief complaint of amenorrhea. Physical examination showed a typically female-appearing girl with a husky, almost masculine voice. The arms and thighs were unusually hairy, and the breasts were hypoplastic and undeveloped. There was a marked hypertrophy of the clitoris. A tiny uterus and both ovaries were palpated; the uterus seemed to be normal in shape and mobility and the ovaries were normal in size. On exploration of the abdomen, the uterus, tubes, and ovaries were plainly identified. The hypertrophied clitoris was excised and a perineotomy was performed. The wounds healed satisfactorily.

After a control period during which 17-ketosteroids, estrogens, gonadotropins, and pregnanediol excretions were determined weekly and body temperature and vaginal cytology were determined daily, cortisone therapy was started with 50 mg. given daily for 60 days. The output of 17-ketosteroids ranged between 40 and 50 mg. during the control period before cortisone was given. A prompt decrease in 17-ketosteroid excretion to 7.5 mg. resulted on the fourth day of treatment. The authors agree with Wilkins that for optimum effect the dose of cortisone should be adjusted to keep the excretion of 17-ketosteroids below 8 mg. daily. It remained below 8 mg. for about 23 days, then rose to levels of 20 or 30 mg., which were maintained for over three months despite the steplike increase in cortisone dosage. Only by the intramuscular administration of 50 mg. of cortisone daily for one week could the excretion of the 17-ketosteroids be decreased to below 8 mg. daily. The oral administration of 100 mg. of cortisone daily was required to maintain the level of 17-ketosteroid excretion at 8 or 10 mg. daily. The oral dose of cortisone and the 17-ketosteroid excretion were maintained at these levels for about six months. At this dosage considerable feminization occurred, with normal development of breasts, cornification of the vaginal smear, regular menstruation, and a decrease in hirsutism. Although the urinary estrogen excretion and the cornification of the vaginal smear showed cyclic changes coinciding with the menstrual periods, no positive evidence of ovulation was obtained during the period of study.

The primary defect in congenital adrenal hyperplasia is the inability of the adrenal cortex to synthesize readily the glucocorticoids, such as hydrocortisone. This defect causes excretion of excessive amounts of corticotropin by the anterior pituitary, to which the adrenal cortex responds by the production of an increased amount of androgenic steroids, resulting in the symptoms of virilism. The excessive secretion of androgens and estrogens suppresses the gonadotropic function of the anterior pituitary. Administration of cortisone inhibits the excessive output of corticotropin, thereby decreasing adrenal secretion of androgen and permitting gonadotropic activity by the pituitary, ovarian secretion of estrogen, and normal actions of estrogens on secondary sex development.

Afibrinogenemia Resulting from Amniotic Fluid Infusion. H. F. Sandmire and B. M. Covalesky. U. S. Armed Forces M. J. 7:1351-1355 (Sept.) 1956 [Washington, D. C.].

Studies in patients with amniotic fluid embolism revealed that patients who survived the initial shock died with hemorrhagic manifestations. Bleeding occurred from the mucous membranes, organ surfaces, and vagina, and the blood at autopsy was liquid. Investigation into the hemorrhagic tendencies of amniotic fluid embolism revealed thromboplastin in the amniotic fluid. The concentration of thromboplastin in amniotic fluid is apparently determined by the degree of fetal exfoliation and is hence variable from patient to patient. Death occurring suddenly in amniotic fluid embolism can be explained by extensive intravascular coagulation, while death occurring two or three hours after delivery is due to postpartum hemorrhage resulting from afibrinogenemia. The available circulating fibrinogen is rapidly used up in the formation of the intravascular clot, and hence afibrinogenemia or hypofibrinogenemia results. Two possible methods of entry of amniotic fluid into the maternal circulation have been suggested. One portal of entry is thought to be through the exposed endocervical veins, which become lacerated during normal labor. The second portal of entry involves a rupture of the membranes somewhere in the upper segment of the uterus, with eventual escape of the fluid through the uteroplacental site.

The authors cite the history of a patient who, they believe, had afibrinogenemia as a result of the entrance of amniotic fluid into the maternal circulation. Postpartum oozing became ominous and responded only temporarily to blood transfusions, but was finally controlled by the intravenous administration of fibrinogen. The authors stress the importance of having fibrinogen available, inasmuch as obstetric hemorrhage is still an important cause of maternal deaths.

PEDIATRICS

Viral Infections in the Embryo. J. M. Adams, H. D. Heath, D. T. Imagawa and others. A. M. A. J. Dis. Child. 92:109-114 (Aug.) 1956 [Chicago].

Experiments were carried out in mice in an attempt to confirm the concept that viral infections of the mother during gestation may adversely affect the developing young. The concept suggests that severe infections in the embryo may result in death, while mild infections may produce abnormalities or the fetus may be born apparently normal. Swiss albino mice were inoculated with a human strain of influenza virus just after mating. When the animals were killed at approximately 18 days of gestation, 168 live embryos were present in 20 mice of the virus-infected group, as opposed to 190 live embryos in 20 control animals. In the virus-infected group there were 10 dead embryos and in the controls there were 5 dead embryos. Among the 10 dead embryos, 2 were smaller than normal, 1 was curled and shorter than normal, 2 showed abnormalities in the cephalic area, and 5 were resorbed. Among the five dead controls, one was small, one was normal, and three were resorbed. No true anomalies or abnormalities were observed in the control group. Thus not only was the pregnancy rate reduced but evidence of abnormalities in the fetuses was increased by inoculation of the mother animals with the influenza virus.

Embryonated hen's eggs that had been incubated for 48 hours were injected with influenza-A virus through the vitelline membrane immediately covering the embryo. The appearance of the body flexion and microencephaly was characteristic of influenza infection 24 hours after the inoculation. After 48 hours the mesencephalon and telencephalic hemispheres were typically almost completely collapsed. The eyes were frequently flattened and misshapen, and the auditory vesicles sometime appeared compressed. Microscopic sections of the infected embryos revealed a distorted and abnormal spinal cord, and the amniotic membranes were thin and flattened. Embryos that received noninfected allantoic fluid developed normally. Virus was recovered from all of the suspensions prepared from dead embryos with typical anomalies. Dilutions of antiserum as high as 1:800 completely protected all embryos against both the teratogenic and the lethal effects following infection after mixture with the virus in vitro. This result did not occur when either normal rabbit serum or control medium was substituted for immune serum. The optimum protection was obtained when antiserum was administered before virus inoculation. The protective effect was less marked when immune serum was given one, two, or five hours after virus infection, and it practically disappeared when serum therapy was delayed until eight hours after virus injection. A 100% incidence of anomalies and death occurred in the control group.

Neonatal Nephritis. L. I. Taft. Australasian Ann. Med. 5:113-117 (May) 1956 [Sydney, Australia].

A survey of 1,200 autopsies, performed at the Royal Children's Hospital in Melbourne from 1949 to 1954, was made in order to determine the incidence and nature of neonatal glomerulonephritis. The histories and pathological findings in two infants (one boy and one girl) in whom the diagnosis of neonatal glomerulonephritis could reasonably be entertained are reported. Both infants were hospitalized when three weeks old, one because of intermittent diarrhea and the other because of vomiting. The clinical manifestations of renal failure in infancy are usually gastrointestinal in type, and antemortem diagnosis of glomerulonephritis is made on the results of laboratory investigations of the urine and serum. This was exemplified by observations on the first infant. The renal origin of the symptoms was suspected in the second infant. Death occurred in the first infant 67 days and in the second 14 days after admission to hospital.

Autopsy in each infant revealed shrunken kidneys with structural deformity, cystic changes, and scarring. The histological appearance resembled that of glomerulonephritis, showing parenchymal damage, cellular infiltration, proliferative phenomena, and fibrosis. Increased cellularity of the tufts, capsular exudate, and adhesions were seen in the glomeruli, with red blood cells and casts in the tubules. Tuft digitation and capillary obliteration had progressed to hyalinization of many glomeruli. Islands of dilated subcapsular tubules were lined by hypertrophic or flattened cells, while other tubules were shrunken and lined by irregular atrophic epithelium. The number of nephrogenic tubules seen indicates that increased nephrogenesis continued after term, probably under the stimulus of renal failure. These and other cases reported in the literature suggest that the disease process is initiated in utero and that the pathogenesis is comparable to that observed in glomerulonephritis in later life, modified by the developmental processes taking place in the kidney at that time. In the same period in which these two cases were discovered, pyelonephritis associated with urinary tract anomalies and/or septicemia was found in 49 babies that had died within the first year of life.

Penicillin V Treatment of Beta-Hemolytic Streptococcal Infections in Children. B. B. Breese and F. A. Disney. A. M. A. J. Dis. Child. 92:20-23 (July) 1956 [Chicago].

Treatment with penicillin V (phenoxymethyl penicillin) was practiced in 110 cases of beta-hemolytic streptococcic infections in children. Unlike solutions of other penicillin salts, the aqueous solution of this preparation is relatively stable in the acid secretion of the gastric juice. It passes through the stomach with little change and shows better absorption from the intestinal tract. All patients were examined by one of the authors, and throat cultures that grew beta-hemolytic streptococci were obtained. If the child was well and the culture negative at the end of six weeks from the start of therapy, he was classified as "cured"; if he became ill up to 60 days after initial therapy, he was classified as a "recurrence"; and if he remained well but the throat culture remained positive or became positive later, he was classified as a "carrier." The drug was dispensed in tablets of 200,000 units (125 mg.). Each patient was given 30 tablets, regardless of age, with instructions to take 3 a day, one on awakening, one at 2 p.m., and one at bedtime.

Four of the 110 patients originally treated were not followed and were excluded from the series. Six of the remaining 106 patients had recurrent attacks, and 17 became carriers at various periods up to 60 days after therapy. Another child developed acute glomerular nephritis on the eighth day. Of the remaining 82 patients, 96% were observed for more than 15 days and 82% for more than 30 days, and all of these were classified as cured. The series contained 56 cases of streptococcic sore throat, 19 pyogenic streptococcic complications (11 cervical adenitis, 4 otitis media, and one each of sinusitis, peritonsilar abscess, vaginitis, and impetigo), and 35 carriers (patients not ill but with positive throat cultures). In all instances in which the patient was clinically ill the response to therapy was that usually expected from penicillin in streptococcic infections; prompt drop in temperature and rapid improvement in the state of well-being. The purpose of the present study is not to discuss the relative value of penicillin V in contrast to other penicillin preparations in the treatment of beta-hemolytic streptococcic infections in children, since the patients as a group are not comparable to those studied previously. With rare exceptions, all the antibiotics and certainly all forms of penicillin are clinically valuable in the treatment of beta-hemolytic streptococcic infections. The authors' results therefore have been judged by rather severe standards. The therapeutic agent must be able to prevent recurrence and to eliminate the streptococcus from the throat for a period more than 21 days, preferably 42 to 60 days. The organism is apparently often held in abeyance but not destroyed by treatment thought to be adequate. A second attack may be a reinfection, but for the present purposes is considered as a recurrence and therefore a therapeutic failure. On the basis of these standards, penicillin V qualifies well as a therapeutic agent against beta-hemolytic streptococcic infections in children. The immediate clinical response was good, and the cultures became negative rapidly. There were no toxic reactions, and the children took the tablets without trouble. Penicillin V given orally appears to be an effective drug for the treatment of streptococcic infections in children.

Staphylococcal Pneumonia in the Newborn: An Epidemic with 8 Fatal Cases. D. W. Beaven and A. F. Burry. Lancet 2:211-215 (Aug. 4) 1956 [London, England].

The authors report on an epidemic of micrococcic (staphylococcic) pneumonia in newborn infants, with eight fatal cases. The nursery involved is the maternity annex of a large private hospital in Christchurch, New Zealand. Overcrowding of nurseries is common throughout the country. Infection of the upper respiratory tract was noticed about the age of 12 to 14 days. On admission, the eight infants in whom the disease was fatal showed striking breathlessness and pallor, which had developed about three days after the onset of the cough. Before death, cyanosis was noted and the temperature fell below normal. Well-marked physical signs were detected in the chest on auscultation. The authors divide the course of the fatal cases into three stages: (1) nasal infection only, with copious mucous purulent nasal discharge, but baby remaining well; (2) infection of the upper respiratory tract, with cough as the main symptom; and (3) pneumonia attended by pallor and breathlessness, often rapidly fatal.

Six of the infants that died underwent radiography of the chest. All six showed evidence of pleural fluid on the right side. Less fulminating cases presented pneumatoceles in an area of consolidated lung; emphysema, diffused or localized; and a spontaneous tension pneumothorax with or without empyema. All six babies had hemorrhagic pneumonia, segmental in distribution and apparently resulting from inhalation. There was a well-marked tendency to suppuration, and the pleural cavity was involved consistently and early. There were no striking lesions in the upper respiratory tract. The nasal fossae contained large amounts of thick mucopus, but the mucosa was usually intact. The middle ear was not involved. There were no gross changes in the larynx or in the trachea to indicate a viral infection. Patients were at first treated with chloramphenicol, but without success. More success was obtained with erythromycin. The dose was initially 20 mg. per pound of body weight daily, given orally in six divided doses, but subsequently, 40 mg. per pound of body weight daily for the first 24 hours was used. Bacteriological studies revealed that many, if not all, of the resistant staphylococci were probably of the same phage pattern (42E/7/73).

DERMATOLOGY

Treatment of Pemphigus with ACTH, Cortisone and Prednisone: Results Obtained in 25 Cases over a Period of Five Years. L. Reznick, W. F. Lever and C. N. Frazier. New England J. Med. 255:305-315 (Aug. 16) 1956 [Boston].

Twenty-five patients with pemphigus were treated at the Massachusetts General Hospital between 1950 and 1954, with either corticotropin (ACTH), cortisone, or prednisone. The patients were followed up to Oct. 1, 1955, or to the time of their death. Fourteen patients had pemphigus vulgaris, 1 had the benign form of pemphigus vegetans (Hallopeau type), and 10 had pemphigus foliaceus. The diagnosis of pemphigus was confirmed in each patient by the demonstration of acantholysis on microscopic examination.

Every patient responded to treatment with various hormone preparations at all times, but very high doses were necessary for the control of some of the exacerbations. An approximately equivalent clinical response was observed with the following daily doses: 20 units of lyophilized ACTH given as a continuous infusion, 40 units of lyophilized ACTH given as an eight-hour infusion, 300 units of lyophilized ACTH intramuscularly, 240 clinical units of ACTH gel intramuscularly, 600 mg. of cortisone orally, and 120 mg. of prednisone (Meticorten) orally. The highest doses administered for the control of exacerbations were 300 units of lyophilized ACTH given intramuscularly, 80 units of lyophilized ACTH given intravenously for 8 hours, 80 units of lyophilized ACTH given intravenously for 24 hours, 300 clinical units of ACTH gel given intramuscularly, 1,500 mg. of cortisone given orally, and 200 mg. of prednisone given orally. Intravenous injections of ACTH were preferred for the control of severe exacerbations, and for maintenance treatment either ACTH gel on alternate days or one of the corticosteroids every day. Of the 14 patients with pemphigus vulgaris, 10 are living; 9 are ambulatory, and 4 of them have been in remission for 49, 43, 25, and 2 months respectively. Four patients died, one of an incidental disease, one of a micrococcic septicemia occurring during a corticotropin withdrawal reaction, and 2 of causes possibly related to the treatment (one of hemorrhages and the other of pulmonary embolism). The one patient with pemphigus vegetans has been in remission for the past 12 months. Eight of the 10 patients with pemphigus foliaceus are living; 7 are ambulatory, and 5 have been in remission for 46, 32, 20, 12, and 3 months respectively. Two patients died, one of an incidental disease, and the other of generalized pemphigus foliaceus while he was not receiving any hormone treatment. Side-reactions to the hormone treatment were common. They included mild mental changes in 11 patients and major psychoses in 2. Bacterial infections occurred in seven patients and resulted in septicemia in two. Vertebral fractures were observed in four patients, all of whom had been given daily large doses of ACTH gel; this method of treatment has since been abandoned. In four patients the withdrawal of corticotropin was followed by a reaction. To prevent withdrawal reactions, ACTH and the corticosteroids should be withdrawn gradually. Evaluation of the clinical response proved to be a better guide to successful treatment than laboratory data. Measurements of the urinary secretion of 17-hydroxysteroids in one patient indicated that a very pronounced hyperadrenocorticoid state must be induced before a severe exacerbation subsides. The same daily dose of ACTH produced a much higher excretion of 17-hydroxysteroids when given as a continuous infusion for 24 hours each day than when given as an intermittent infusion for 8 hours daily.

UROLOGY

Urethrotrigonitis in Women. R. F. Fortuño and B. Rodríguez Lucca. Bol. Asoc. méd. Puerto Rico 48:204-206 (May) 1956 (In Spanish) [Santurce, P. R.].

Urethrotrigonitis is frequent in women. Trichomonas vaginalis is the causal organism in many cases. The symptoms include frequent micturition, dysuria, a burning sensation during urination, urgency to void, feeling of incomplete emptying of the bladder, and hematuria. Symptoms may flare up during or after menstruation. Dyspareunia and pain in the groin, thighs, and iliac fossa may be the predominant or only symptom of this disease. Twenty-five patients were observed in the outpatient department of the San Juan City Hospital. The diagnosis was based on the history and confirmed by cystoscopic examination. None of the patients was suffering from any other disease of the urinary tract. The treatment was as follows: The bladder was emptied and two ounces of a 20% solution of Furacin (nitrofurazone) instilled into it. A suppository of Furacin was placed in the urethra after instillation and held in place for five minutes. The patients were then sent home with instructions to void one hour later. The treatment was given on 10 consecutive days to 15 patients and once a week for two and a half months to 10 patients. Three patients had moderate allergic reactions with aggravation of the symptoms, itching, and edema of the vulva. One had gross hematuria. The reaction was controlled by discontinuing the treatment and giving antihistaminic drugs. The treatment failed in three patients with the acute form of the disease. These patients had a transurethral resection of the neck of the bladder at a later date. Nineteen patients were completely cured upon completion of the treatment. Eight had a recurrence of the disease between three and five months after completion of treatment. The recurrences were permanently controlled by repetition of the treatment. The patients remain cured up to the present, as shown by the follow-up observations.

Treatment of Renal Colic. L. Risholm. Urol. Internat. 2:361-368 (No. 6) 1956 (In English) [Basel, Switzerland].

Posterior splanchnic block was used for routine treatment of severe renal colic in 200 patients admitted to the department of surgery of the University Hospital of Uppsala, Sweden. The anatomic conditions make it simple to block all pain-conducting nerves from the upper urinary tract by conduction anesthesia. All the pain-conducting fibers from the renal pelvis, where the pain probably arises, pass through the celiac plexus and the splanchnic nerves to the spinal cord. The afferent fibers in the vagus nerves do not conduct pain. Posterior splanchnic anesthesia has definite advantages when compared with segmental paravertebral anesthesia; in particular, it is easier to carry out, and that is why it is recommended. The needle is introduced immediately below the 12th rib, about 7 cm. from the midline, and is directed 30 to 40 degrees medially and 10 to 20 degrees cranially. At a depth of from 7 to 8 cm., the point of the needle meets a bony resistance, the dorsolateral aspect of the vertebral body. The needle is then withdrawn a little and is redirected

PATHOLOGY

Needle Biopsy of the Liver in Cirrhosis: Diagnostic Efficiency as Determined by Postmortem Sampling. H. Braunstein. A. M. A. Arch. Path. 62:87-95 (Aug.) 1956 [Chicago].

While liver biopsy by the transcutaneous needle method has become a widely accepted diagnostic procedure in the diagnosis of conditions diffusely affecting the liver, such as hepatitis, fatty liver, and amyloidosis, its efficiency in the demonstration of focal lesions and those with less uniform characteristics has been questioned. Investigation by a sampling technique at the time of postmortem examination would aid in evaluating the accuracy of diagnosis of various types of portal cirrhosis by needle biopsy. Accordingly, the livers of 30 patients with various forms of portal cirrhosis were obtained at autopsy and 18 needle specimens taken from different portions of each liver with the Vim-Silverman needle. The technique used has been described by Billing and associates. It consisted of procuring 12 specimens from different but standardized areas in the right lobe and 6 from the left lobe. Each adequate needle sample was classified as to the type of cirrhosis and severity of the lesion, on the basis of sections prepared in standard fashion and stained with hematoxylin and eosin and, where necessary for determination of degree of fibrosis, the Masson trichrome stain.

Definite diagnosis and ultimate classification rested upon gross examination of the lesion at the time of autopsy and microscopic study of the postmortem sections, which usually consisted of two or three blocks measuring 1.5 cm. in diameter. A total of 507 adequate needle samples were obtained, namely, 224 in 13 cases (autopsies) of nutritional cirrhosis, 131 in 8 cases of postnecrotic cirrhosis, and 152 in 9 cases of posthepatitic cirrhosis. Of the 507 adequate samples, only 10 failed to reveal cirrhosis. In cases of nutritional cirrhosis the accuracy of diagnosis was 100%. The degree of the fibrosis revealed a remarkable uniformity in all areas of the liver. In cases of post- atitic and postnecrotic cirrhosis the accuracy of recognition presence of cirrhosis was roughly 96%, but in many of ·ly negative samples some fibrosis was present. In the forms of cirrhosis, there was considerable variation in ne intensity of fibrosis, and the biopsy method would therefore be of little value in the appraisal of severity. It is concluded that needle liver biopsy represents a singularly accurate method of diagnosing cirrhosis of all three types. A liver biopsy that fails to demonstrate cirrhosis or fibrosis rules out cirrhosis with reasonable certainty. As a means of estimating the severity of the process, accuracy may be assumed only in the case of nutritional cirrhosis.

Massive Hematemesis Without Gross Lesion. J. F. Kuzma. Am. J. Gastroenterol. 26:150-152 (Aug.) 1956 [New York].

Massive upper gastrointestinal hemorrhage is a cause of great concern to the pathologist who has to explain the mechanism of hemorrhage or demonstrate its anatomic cause. Many hospital reports refer to hemorrhage of undetermined origin, but massive bleeding from the stomach should be traceable to an anatomic lesion. Material obtained from patients with upper gastrointestinal hemorrhage but otherwise in good health whose stomachs were available for study either as surgical or as autopsy specimens has been reviewed in an attempt to find an anatomic explanation for the hemorrhage. Superficial erosions were discovered in most of the stomachs. The reason for failure to identify these erosions grossly lies in the fact that many of them are covered or filled with fibrin and pseudomembrane. Moreover, these microscopic erosions commonly begin in the furrows of the gastric mucosa and are not readily seen. The pseudoepithelial layer of the stomach may play an important part in developing a surface membrane, which fills the zones of erosion. There is a strong suggestion that many of these erosions are located in the area of the lesser curvature. They occur primarily in stomachs otherwise designated as those of hypertrophic gastritis. Only one case was found in an atrophic mucous membrane. The cause of these microscopic and near-microscopic erosions has not been determined.

The Behavior of Carcinoid Tumors of the Intestinal Tract. D. M. Spain. Am. J. Gastroenterol. 26:162-169 (Aug.) 1956 [New York].

Benign carcinoid tumors may produce a variety of manifestations as a result of local involvement of the intestinal tract, e. g., obstruction, intussusception, diarrhea, hemorrhage, pain, and weight loss. Carcinoid tumors are frequently malignant, but long survival in the presence of metastases is not uncommon. The syndrome associated with malignant carcinoid tumor consists of predominantly right-sided valvular endocardial fibrosis, a peculiar type of skin telangiectasia, skin cyanosis and blushing secondary to vasomotor changes, and asthma-like symptoms due to bronchoconstriction. The substance responsible for this syndrome is believed to be 5-hydroxytryptamine, regarded as a specific hormone of the enterochromaffin cell system that is also elaborated in great quantities by carcinoid tumors.

Changes in the Intramural Coronary Branches in Coronary Arteriosclerosis. O. Saphir, L. Ohringer and R. Wong. A. M. A. Arch. Path. 62:159-172 (Aug.) 1956 [Chicago].

Factors that have been regarded as important in arteriosclerosis and atherosclerosis include heredity, hypertension and obesity, and those related to endocrine disturbances, such as steroid hormone relationships, sex, thyroid dysfunctions, diabetes, and gout. In the past, inflammatory factors were considered as possible causes, but now the weight of evidence seems to favor an abnormal cholesterol metabolism as of prime importance. The old concept of inflammation as at least one factor in the causation of coronary arteriosclerosis is discussed. The studies described were designed to determine whether what appears as primary coronary artery sclerosis may not, in certain instances, actually represent the end-stages of an inflammatory process. Since it was felt that the main coronary arteries might no longer show the pathogenesis of these lesions, the intramural branches of the coronary arteries were examined. Although it had been planned to study the myocardium in instances of coronary arteriosclerosis in patients up to the age of 40, it was thought more profitable to include also patients up to 50 years of age, especially as the increase in the incidence of arteriosclerosis that the authors have observed during the last 15 years involves particularly the age group from 40 to 50 years.

The myocardiums of 100 patients were examined with the aid of the microscope. Only those cases were selected for study in which the final autopsy diagnosis was coronary arteriosclerosis or coronary atherosclerosis, with or without myocardial changes. There were 32 females and 68 males. Remnants of inflammatory changes were found in the intramural branches of the coronary arteries in 82. These changes consisted of perivascular cellular infiltrations, perivascular or adventitial fibrosis, intimal fibrosis and hyalinization, the arteritis obliterans type of lesions, and fibrous changes in the media. In a number of instances, these changes were characteristic of old periarteritis or panarteritis. Autopsy findings and a review of the clinical histories disclosed evidence of endocarditis in 12 cases, in 8 of which it was most probably rheumatic in origin. Ten patients volunteered histories suggesting hypersensitivity or showed autopsy findings interpreted as allergic in origin. Six other patients showed changes in the intramural branches of the coronary arteries that were indistinguishable from those seen in the group with hypersensitivity. The relation of the changes in the smaller branches of the coronary arteries to those in the large branches is discussed, and it is suggested that the intramural coronary artery disease may provide a clue to the nature of the changes in the large coronary arteries that are indistinguishable from primary arteriosclerosis and atherosclerosis. The question is raised whether perhaps the increase in coronary arteriosclerosis in the younger age group may not be associated with hypersensitivity related to the common use of antibiotics and chemotherapeutics.

BOOK REVIEWS

Psychoanalysis and Psychotherapy: Developments in Theory, Technique, and Training. By Franz Alexander, M.D., Director, Chicago Institute for Psychoanalysis, Chicago. Cloth. $4.75. Pp. 299. W. W. Norton & Company, Inc., 55 Fifth Ave., New York 3, 1956.

In this book the author comprehensively presents the developments of the past 20 years in the theory and technique of psychoanalysis. His purpose is to clarify prevailing views and practices and to call attention to the discrepancies existing between our theoretical model of procedure and what actually takes place in treatment. Of special interest are his views in regard to the application of psychoanalytic theory to those forms of psychotherapy that differ from traditional analysis. The author first discusses the impact that he believes psychoanalysis has made on Western culture. He then traces, in a remarkably concise manner, the development of psychoanalytic theory from its inception to the present. He reviews those aspects of theory that have enjoyed general acceptance and then traces early modifications of theory as they oscillated between an overemphasis on one of two basic therapeutic factors: psychoanalysis as primarily a cognitive process (ego-analysis) and psychoanalysis as primarily a meaningful emotional experience. In discussing more recent developments, he clarifies his view of the transference relationship as a corrective emotional experience and the axis around which present analytic technique revolves. For those versed in psychoanalysis the only ideas that may appear to be new or unfamiliar are those the author proposes in his discussion of the countertransference phenomenon and the relationship of classic analysis to other forms of psychotherapy.

With regard to countertransference, the author proposes that the analyst should attempt to replace his spontaneous countertransference reactions with attitudes that are consciously adopted to create the type of emotional climate the patient's dynamic situation demands. In discussing more recent forms of psychotherapy, he states that they differ from the classic technique in quantity but not in their basic characteristics. He points out the value of the shorter forms of supportive and uncovering psychotherapy for patients not amenable to the classic technique. He deals extensively with the therapeutic implications of regression and with the technical problems regarding the frequency of interviews and planned interruptions of treatment. One chapter is devoted to the controversial issues that arose in response to "Psychoanalytic Therapy," written by the author of the present book and Thomas French in 1946. The last quarter of the book is devoted to the problem of psychiatric training in psychoanalytic institutes and medical schools. In general, it is gratifying to note the author's emphasis on empirical data as the source of modification in analytic theory rather than on a priori assumptions found in some psychoanalytic work. It is interesting, however, that in his praise for psychoanalysis the author seems to ascribe to it almost all that has been learned of the psychology of man. He refers to philosophy only when it agrees with analytic theory; he gives only a passing nod to sociology and anthropology and does not mention the vast field of academic psychology at all. One cannot help wondering at this omission.

Pathologische Anatomie der raumbeengenden intrakraniellen Prozesse. Bearbeitet von K. J. Zülch und E. Christensen. Band III, Handbuch der Neurochirurgie. Herausgegeben von H. Olivecrona und W. Tönnis. Cloth. 298 marks. Pp. 800, with 473 illustrations. Springer-Verlag, Reichpietschufer 20, (1) Berlin W. 35 (West-Berlin); Neuenheimer Landstrasse 24, Heidelberg; Göttingen, Germany, 1956.

This outstanding book is divided into two sections. The first, Biology and Pathology of Brain Tumors, is by Zülch and occupies the greater part of the volume. The second deals with the pathology of intracranial hemorrhage; it is only 30 pages long and is by Christensen. The first section is representative of German medical writing at its best. It is typical of the scientific work that was expected of German authors over 25 years ago but of which we have seen so little in more recent years. This volume is a classic and will undoubtedly be the standard reference work on this subject for many years to come. The literature on the subject from the entire world has been carefully and intelligently reviewed. The work and opinions of all investigators worthy of consideration have been presented. The author has stated his own opinion and his reasons for differing with the views of others. The bibliography is unusually complete; the author and the publisher are to be congratulated on having adopted the alphabetical and columnar style of arranging the names of authors cited in the bibliography. This makes for much easier reference than the usual German style. It is still difficult, however, to distinguish the different works of two different authors with the same last name. Each type of tumor is taken up separately. The author has followed the classification of Percival Bailey of Chicago quite closely. He has recognized, as many neuropathologists have, that there is a definite difference in behavior between the astrocytomas of the cerebral hemispheres and those of the cerebellum. He has endeavored to distinguish between these two types of tumors by grouping the cerebellar ones with the polar spongioblastomas, which commonly involve the neural axis and the optic nerves and chiasm. This does not seem to be a proper or satisfactory solution to the problem. On the other hand, the grouping of the various tumors of peripheral nerves, referred to by others by such terms as perineural fibroblastoma, neurofibroma, and schwannoma, seems entirely justified.

Each type of tumor is taken up similarly. The author first discusses the historical aspects and its place in the classification; the frequency, sex and age incidence, and common site of origin are then presented. He next takes up the gross and microscopic appearance of the tumor. These aspects are well and profusely illustrated. The tendencies, if any, toward degenerative changes, recurrence, and metastasis are then considered. Lastly, the author briefly discusses the pathological differential diagnosis, the prognosis, and therapeutic possibilities. In addition to the various tumors of the glioma group, the neurinomas, meningiomas, angioblastomas, pituitary tumors, blood vessel tumors and malformations, and metastatic tumors, he discusses parasitic and granulomatous involvement of the brain and arachnoiditis. He concludes with a brief presentation of a few points concerning technical methods for preserving, sectioning, and staining these tumors. The second section is not comparable to the encyclopedic study of tumors that is presented in the first. It consists of a brief discussion of epidural, subdural, subarachnoid, and intracerebral hemorrhage. The publisher is to be congratulated on the splendid manner in which this book is presented. The printing is excellent, and the illustrations are well reproduced. Everyone having to do with tumors of the brain should have this volume readily available, although the high price may make that impossible.

The Practice of Psychiatry in General Hospitals. By A. E. Bennett, M.D., Associate Clinical Professor of Psychiatry, University of California, School of Medicine, San Francisco, Eugene A. Hargrove, M.D., Assistant Professor of Psychiatry, University of North Carolina, School of Medicine, Chapel Hill, and Bernice Engle, M.A., Research Associate, Department of Psychiatry, University of California, School of Medicine, with contributing authors. Cloth. $4. Pp. 178. University of California Press, Berkeley 4, 1956.

In addition to developing psychiatric departments in several general hospitals, Dr. Bennett and co-workers conducted a survey that disclosed that less than 1% of patients suffering from mental illness were accommodated in American and Canadian hospitals. They incorporated their findings into a scientific exhibit that attracted much attention and stimulated many inquiries. They have prepared this book from the material collected for the exhibit; here they consider the main problem connected with installing and operating a psychiatric department within a general hospital. They believe that "as the advantages of the psychiatric unit are better understood patients will generally be admitted to general hospitals for treatment of acute mental illness to the same extent as for other acute medical illnesses, disorders and accidents; that modern medicine will eventually accept its responsibility to treat the entire person."

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

The foreword, introduction, and preface of this volume are followed by 10 chapters and a general index. At the end of each chapter there are lists of references. Although the authors are dedicated to the integration of psychiatry into the practice of medicine in general hospitals, their organization of this book does not describe the process. The reader will gain practical information on the staffing of a psychiatric unit, training programs, administration, architecture, psychiatric referral, medicolegal aspects, health insurance, the day hospital, and special treatments. Sections on these separate subjects are contributed by several authors, some of whom have special competence in the problems pertaining to the hospital practice of psychiatry. These separate chapters are well written and apparently are intended as sources of reference when the establishment of a psychiatric unit in general hospitals is under consideration. The value of the book would be greatly enhanced by the addition of a chapter describing the functioning of the departments of psychiatry in one or more hospitals. It is also hoped that in a subsequent edition the authors will describe in detail the various improvements in medical care they have observed in general hospitals in which psychiatric units have been functioning for some time. Such observations would be of practical interest to general practitioners and medical specialists.

Human Perspiration. By Yas Kuno, M.D. Publication 285, American Lecture Series, monograph in Bannerstone Division of American Lectures in Physiology. Edited by Robert F. Pitts, M.D., Ph.D., Professor of Physiology and Biophysics, Cornell University Medical College, New York. Cloth. $9.50. Pp. 416, with 76 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England, Ryerson Press, 299 Queen St., W., Toronto, 2B, Canada, 1956.

This study of the present knowledge of perspiration is based primarily on the personal observations of the author. Although derived from a similar volume written in 1934 by the same author, the book has been radically changed in both style and context. The writer believes that sweating deserves far more consideration, from both physiological and social aspects, than has usually been accorded to it; and his reasons are advanced in a lucid and convincing manner. The individual chapters include detailed descriptions of the development, anatomy, chemistry, and physiological mechanisms of the human sweat apparatus. Additional chapters describe regional and general forms of sweating, as well as their diverse relationships to the chemistry of the blood, and the influence of drugs, temperature, and stress. Of particular interest are the author's concepts of the skin chloride shift in sweating and the reabsorption of sweat in the sweat duct. The author presents a method for the suppression of local hyperhidrosis; this method, consisting of the administration of a 10% solution of formaldehyde by iontophoresis, has its drawbacks. The discussion of the significance of water debt during physical exercise in hot weather is of great interest. The book is well written and printed, and the illustrations and tables are both adequate and clearly reproduced. Although the volume is small, it is filled with valuable information.

Clinical Selections in Dermatology and Mycology. By Frederick Rehm Schmidt, A.B., M.D., Associate Professor of Dermatology, Northwestern University Medical School, Chicago. With contributions by 36 specialists from various lands. Cloth. $10.50. Pp. 505. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England, Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1956.

Since each contribution to this volume is written by an expert on a specific disease, this is not a textbook for the student but rather a summary of the knowledge and experience of an authority on a subject, condensed and maturely presented both for the practicing physician interested in a special topic and for the dermatologist. No attempt is made to present the material in an integrated or coordinated form. This is not a disadvantage, however, inasmuch as the contributions cover the important subjects in a thorough and thoughtful manner and properly emphasize controversial opinions and original ideas. Some of the more important contributions include the chapters on nutritional dermatoses, the collagen diseases, and the pigmentary dermatoses. Original methods of treatment are emphasized, and the use of simple, practical remedies is advised whenever possible. A large portion of the book deals with the pathogenesis, diagnosis, and therapy of fungous diseases, including those prevalent in tropical regions. The psychosomatic dermatoses are not neglected; and the role of enzymes, vitamins, and diet in the cutaneous economy is also described. For the most part, the discussions are written with simplicity and clarity of style, and the bibliography is adequate. This reference book should be welcomed by those interested in both the simple and the complex aspects of dermatology and mycology.

Allgemeine Theorie der menschlichen Haltung und Bewegung als Verbindung und Gegenüberstellung von physiologischer und psychologischer Betrachtungsweise. Von Dr. F. J. J. Buytendijk, o. Professor der Psychologie der Reichsuniversität Utrecht, Utrecht, Holland. Titel der Originalausgabe: Algemene Theorie der menselijke Houding en Beweging, 1948. Cloth. 39.60 marks. Pp. 367, Springer-Verlag, Reichpietschufer 20, (1) Berlin W35 (West-Berlin); Neuenheimer Landstrasse 24, Heidelberg; Gottingen, Germany, 1956.

This book, competently translated from the Dutch, reflects the author's thorough knowledge of physiology, psychology, and philosophy. He endeavors to give the theoretical foundation of the movements and postures as purposeful acts; and, though he emphasizes the merits of the Gestalt theory, he shows that the traditional physiological and psychological investigations do not provide an adequate explanation. In addition to an analysis of various types of voluntary and reflex movements, the author discusses, in a fascinating chapter, the facial expressions. A section on the genesis of human movements, which stresses also the learning processes, and one on the sex and age differences of movements conclude this informative and challenging book. The author's phenomenological analysis of the movements and his discussion of the relevant physiological, psychological, and clinical literature should make fascinating reading for physiologists and neurologists. His holistic approach to the problem of human behavior is related to that of the Heidelberg neurological school (vs. Weizsäcker). The printing and binding are excellent.

The Office Assistant in Medical or Dental Practice. By Portia M. Frederick, Instructor, Medical Office Assisting, Long Beach City College, Long Beach, Calif., and Carol Towner, Executive Assistant, Department of Public Relations, American Medical Association, Chicago. Cloth. $4.75. Pp. 351, with 55 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, England, 1956.

This book is a manual of instruction for medical and dental office assistants. All the functions of an office assistant are covered, from those that make the occupation a career to bookkeeping and banking. Specific instructions and modes of conduct in meeting patients and handling telephone calls are stressed. The importance of a good "office girl" to a physician or dentist is also stressed. Record-keeping, handling of mail, and office appointment systems are well discussed. There are chapters on the techniques of sterilization, injection, the care of instruments, and administrative duties. Emphasis is placed on the importance of all possible aids to the practitioner in saving time and pleasing the patients. There is much information about medical societies and their organization that should be of help to an office assistant. The authors are well qualified to present this material, and they have done so in easily readable fashion. The book is well illustrated and can be highly recommended to office assistants.

Proctology. By Harry E. Bacon, B.S., M.D., Sc.D., Professor and Head Department Proctology, Temple University Medical School, Philadelphia, Stuart T. Ross, A.B., M.D., F.A.C.S., Attending Proctologist, Nassau Hospital, Mineola, New York, and Porfirio Mayo Recio, B.S., M.D., M.Sc., Assistant Professor Surgery, College of Medicine, University of Philippines, Manila. Portions of this book were published previously under title "Essentials of Proctology," by Harry E. Bacon, 1943. Cloth. $10. Pp. 441, with 233 illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; 2083 Guy St., Montreal, Canada, Pitman Medical Publishing Co., Ltd., 39-41 Parker St., Kingsway, London, W.C.2, England, 1956.

This excellent volume is designed for the medical student, general practitioner, and general surgeon, but it is also a valuable addition to the library of the proctologist. Illustrations are clear-cut and informative. Especially helpful to the medical student are the tables of differential diagnosis taken from earlier works of the senior author. The authors have given some attention to the etiological importance of anal infection in the common anorectal disorders, such as fissure, hemorrhoid, abscess, and fistula. The inclusion of an excellent chapter on intestinal parasites is timely and appropriate.

QUERIES AND MINOR NOTES

TUBERCULOSIS CASE-FINDING IN TEACHERS

To the Editor:—*The teachers in the school district in which I am the doctor are compelled to have an x-ray of the chest every year. The superintendent wants me to find out if there is any danger in having annual chest x-rays. Would there be any difference whether the standard or the miniature x-ray equipment were used? Is there any possibility of these annual x-rays stimulating the growth of latent cancer cells? Would the factor of an individual being under x-ray therapy, or having had or planning to have diagnostic x-ray studies, be of any great consideration? Would you advise any other means for the detection of tuberculosis in this type of adult population?*

John F. Smith, M.D., Monterey Park, Calif.

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—There is no available evidence to indicate that the x-ray exposure for an annual film of the chest is in any way harmful. The recent writings on this subject have pertained to those who are exposed to x-rays a great deal in their work and those who receive x-ray treatment for various conditions. There would be no difference whether standard or miniature x-ray film equipment were used, as the amount of exposure is extremely small in both procedures. No evidence is available to suggest the possibility that the making of annual x-ray films stimulates the growth of cancer cells. It is not unusual to make periodic x-ray film inspections of the chests, seeking evidence of pulmonary metastases of persons who are under x-ray therapy for malignancy elsewhere in the body. Among teachers, or any other group, the best procedure for the detection of tuberculosis is giving all members the tuberculin test to identify those who are harboring tubercle bacilli. The reactors have x-ray film inspection of the chest periodically to detect gross lesions that may evolve while the disease is still in the silent stage. It is only present tuberculin reactors and those who subsequently become reactors who develop clinical tuberculosis. Therefore, there is no reason to make periodic x-ray film inspections of the chest for tuberculosis of those who are uninfected and who do not react to tuberculin.

This procedure is widely used and recommended by the Committee on Tuberculosis of the American School Health Association, in cooperation with tuberculosis and health associations in several states, where schools are officially certified on the basis of tuberculosis control work in progress. The details of this program may be obtained from Dr. A. O. DeWeese, Executive Secretary, American School Health Association, Kent University, Kent, Ohio.

Answer.—The amount of total body radiation received during a single chest x-ray is only a small fraction of the limit considered tolerable by the National and International Commissions. There are not sufficient data on the difference in exposure between standard and miniature x-ray equipment. There is no evidence to make it seem likely that doses of radiation in this range will be carcinogenic. At the present time a chest x-ray is the best method for detecting early pulmonary tuberculosis in individuals with a positive tuberculin reaction.

DIATHERMY APPARATUS

To the Editor:—*Are there any harmful rays emitted by a diathermy machine the specifications of which are 110 volts, 60 cycles per second, 7 amperes? The operator stands next to the machine, or within half a foot of it.*

M.D., Pennsylvania.

Answer.—*It is assumed that the inquirer is asking about* either a short wave or microwave diathermy apparatus. Diathermy apparatus is intended to provide energy transmitted by electromagnetic waves to the patient for the purpose of heating body tissues. In properly constructed diathermy units, the emission of such energy through the cabinet is so negligible that for all practical purposes there is not even the mildest heating effect on the operator or other persons contacting or standing in close proximity to the cabinet of the apparatus.

MULTIPLE SCLEROSIS VACCINE

To the Editor:—News Facts, *a publication of Toronto, Canada, states that a Dr. Antonina Shubladze at the Soviet Institute of Virology has perfected a vaccine for curing multiple sclerosis and that it is manufactured and distributed by the Kharkov Serum and Vaccine Institute in Moscow. A patient wishes to either confirm or refute the existence of such a vaccine, and, if such a vaccine exists, he would like to have the address of a distributor in the United States so that it could be made available to him.*

M. D., Nebraska.

Answer.—This inquiry undoubtedly refers to a preparation manufactured and distributed from the Metchnikoff Institute in Kharkov, where it is called the "Vaccine of Margoulis and Choubadze." Its nature has been carefully studied in the United States, but whether it fulfills the criteria of a vaccine for multiple sclerosis is extremely dubious, and there is no evidence at all to suggest that it can cure cases of that disease. It is not, as far as is known, distributed in the United States. The proponents of the preparation, in the instructions that accompany it, recommend its use in early cases of multiple sclerosis and in encephalitis. There are, of course, at least two separate diseases and encephalitis may be caused by a host of recognized and unrecognized organisms and conditions.

To limit this discussion to multiple sclerosis, the printed instructions also state that "some early cases may be helped." In the judgment of this consultant, that statement says nothing, since spontaneous remission characterizes early cases of multiple sclerosis. Brickner (*Bull. Neurol. Inst. New York* 4: 665, 1936) and Putnam (*J.A.M.A.* 112: 2488, 1939) studied over 100 reports of treatments for multiple sclerosis and showed that the reported improvement corresponded almost exactly (48%) with the frequency with which early cases go into spontaneous remission.

The preparation of Margoulis and Choubadze was studied at the department of zoology, Rutgers University, which reported (De Falco: Personal communication, 1956) that the material gave a weak protein test and was a homogenate, probably of brain. The supernatant portion faintly reacts to antiserums for rat and mouse but does not react to pig, dog, sheep, chicken, horse, human, rabbit, or hamster antiserums. It is probable that the material is of rodent origin, not necessarily rat, as demonstrated by the naphylactic death of all of seven guinea pigs two to five minutes after they were given rat serum intravenously four weeks after sensitization with two doses of the "vaccine" of 0.25 cc. given on alternate days. The available data do not justify the use of this material, except for investigational purposes by the qualified persons. This is emphasized by Tore Broman (Personal communication, 1956), professor at Göteborg, under whose direction Sigvard Flodmark and Arne Linde have been conducting clinical studies of the Margoulis and Choubadze preparation. There is evidence that patients treated with it develop antibodies against mouse serum, and Broman believes there is at least a theoretical possibility of inducing an encephalomyelitis. His comment, with which this consultant is in complete agreement, is that the chances for benefit are small compared with the possibility of doing serious harm.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

TRANSFUSIONS AND THE HEMOGLOBIN CONTENT

To the Editor:—*The following statement appeared in an abstract of a lecture by Dr. Howard R. Bierman, April 12, 1955: "More transfusions are required to raise the Hgb content from 11 to 14 Gms. than to raise it from 2 to 11 Gms." I could not find an explanation in the literature available to me.*

Hamza I. Munib, M.D., Amarillo, Texas.

Answer.—In context, the statement emphasizes the practical point of maintaining a physiologically sufficient, although reduced, hemoglobin level in patients with anemia due to neoplastic diseases, because of the greater expenditure of effort and blood to return the hemoglobin to the normal 100% level. Little, if any, added value has been demonstrated by transfusing to normal or even polycythemic levels over that of maintaining a comfortable and sufficient hemoglobin level. In some patients with severe anemia due to the leukemias, it has often been observed that one or two units of blood will initially cause far greater rises in hemoglobin levels than an equivalent amount of the blood when the hemoglobin level is already elevated. Many mechanisms are probably involved, a few of which can be mentioned. The total blood volume space is contracted in proportion to the severity of the anemia (McMichael and others: *Lancet* 1:637, 1943). Thus the initial replacement of blood would appear to correct the anemia more efficiently than subsequent transfusions with an expanding blood volume space.

Many patients with neoplastic diseases, particularly the leukemias, often maintain a depressed hemoglobin level for prolonged periods. Apparently the increased rate of erythrocyte destruction is kept in partial compensation by an increased erythropoietic activity, the equilibrium of which determines the hemoglobin level that will be maintained (Crosby and Akeroyd: *Am. J. Med.* 13:273, 1952; Finch and Coleman: *J. Clin. Invest.* 32:567, 1953). It is known that erythropoiesis is most active at the lowest hemoglobin levels and would therefore be of greater assistance at the lower rather than the higher levels if the hemolytic component is brought under control (Dacie: The Haemolytic Anaemias: Congenital and Acquired, Grune & Stratton, Inc. 1955, p. 15). This is further supported by greater reticulocytosis and the presence of normoblasts at the lower levels. On the other hand, transfusions at elevated hemoglobin levels tend to depress erythropoiesis (Boycott and Oakley: *J. Path & Bact.* 36:205, 1933).

ATTACKS OF GASPING FOR AIR

To the Editor:—*For five years, periodically, a college graduate, aged 31, has awakened at night from sound sleep gasping for air. These episodes occasionally occur during the day if he happens to be napping. After his first college year he enlisted in the Marines and was sent to the Pacific theater, where he participated in combat during the entire campaign and was in the first wave that landed on Okinawa. His first symptoms happened on that island. From Okinawa he flew to Guam, where he had another attack. On returning to the United States, he went back to college, graduating in 1952 with a major in physical education and English. At the present time he is a coach in a high school. Last summer an electrocardiogram was made. The cardiologist reported that everything was within the normal level and that he could run a mile if he wanted to. A roentgenogram was normal. He is married and the father of six children. His married life seems to be happy. He has been seen by two colleagues, and the only conclusion we reached was that he is suffering from hyperventilation syndrome. We have been unsuccessful in reducing the frequency and severity of the attacks. Please advise how to cope with this case.* M.D., Wisconsin.

Answer.—There are two possibilities that must be considered in explaining these symptoms: (1) cardiac disease and (2) a hyperventilation syndrome. Cardiac disease would seem to have been pretty well excluded by the fact that the patient has no abnormal heart sounds, the fact that x-ray examination shows no enlargement of the heart, and the fact that the electrocardiographic tracings are within normal limits. In addition, the patient is only 31 years of age. The clinical history certainly would suggest that the patient's difficulty is due to a hyperventilation syndrome. There are many factors that would account for such a condition. First of all, the original attack occurred while the patient was in Okinawa, where he was undoubtedly under emotional strain. It is also interesting to note that his occupation is of such a type that he is subject to great emotional stress from time to time. It would be advisable to have the patient try breathing into a paper bag, to see if this will control his attacks. If this does not prove successful, it might be advisable for the patient to consult a psychiatrist to aid in dealing with his problem.

"TRUTH SERUM"

To the Editor:—*Please give an explanation of the term "truth serum" as it appears in the lay press.*

William K. Owens, M.D., Pulaski, Tenn.

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—So-called truth serum is not a serum, but, as stated by McCartney in his book, "Understanding Human Behavior" (New York, Vantage Press, Inc., 1956), "it is the injection of a drug so that the patient can recall a repressed memory." This technique, called narcosynthesis, came into general use during World War II. A solution of thiopental (Pentothal) sodium or amobarbital (Amytal) sodium is slowly injected intravenously until conscious control is lost, and then the subject is questioned about past experiences. Without conscious censorship the person is apt to tell the "truth."

Answer.—Truth serum usually means a form of barbiturates for intravenous administration given slowly, so that the individual will respond to questioning but his inhibitions will be dulled or removed. An interesting chapter entitled Narcoanalysis for Criminal Interrogation, pages 945 to 979, can be found in "Legal Medicine," edited by Gradwohl (St. Louis, C. V. Mosby Company, 1954).

ENTERITIS IN URANIUM CAMPS

To the Editor:—*In regard to the query and minor note "Enteritis in Uranium Camps," in* The Journal, *June 30, 1956, page 931, the reason might well be arsenic in the water. Arsenic is often found in the regions of mines of this nature and, when taken in small quantities, causes severe enteritis with weight loss. It would be advisable to have chemical analyses of the water used in cooking, for arsenic as well as for other minerals.*

Leland Fuller, M.D.
900 S. Central Ave.
Lodi, Calif.

The above letter was submitted to the consultant who answered the query referred to, and his comments follow.—Ed.

To the Editor:—*Although enteritis tends to be associated with arsenic more as an acute manifestation than on chronic exposure—and the reported condition appears to fall in the latter category—it would seem well to inquire into the possibilities of arsenic absorption in these mines, through analysis not only of the water but also of the urine. However, the probability of arsenic being the cause is low, as reports of such cases are rare, even where arsenic is associated with minerals being mined, and as other symptoms pointing to arsenic as the cause would be expected.*

SURGICAL SPONGES AND HEPATITIS

To the Editor:—*At our hospital the surgical sponges are prepared manually from bulk gauze. After use in surgery they are thoroughly washed, dried, refolded, and autoclaved for repeat use. Is this a safe method of handling surgical sponges? My immediate concern is the possible transmission of homologous serum hepatitis.* *C. R. Heinzerling, M.D., Chaska, Minn.*

Answer.—Although the etiological agent in serum hepatitis is believed to be a virus, it has not been isolated. All known viruses are destroyed by proper autoclaving cycles (121 C or 250 F for 20 to 30 minutes). There is no reason to suspect that sponges, prepared for repeat use as described above and properly autoclaved, would transmit the infectious agent.

« Washington News »

U. S. Employee Health Insurance Studied Further • •
New Center Promotes Research in Problems of Aged
Federal-State Rehabilitation Teamwork Stressed • •
Russian Medical Publications to Be Translated • •

STUDIES OF U. S. EMPLOYEE HEALTH INSURANCE

Various federal agencies are now making cost estimates for carrying out a payroll deduction plan of basic health insurance for federal workers. The data are being gathered by the General Accounting Office (GAD) for the House Civil Service Committee, which is doing a study on the advisability of legislation in this field for the 85th Congress convening Jan. 3. In the last session of Congress, the administration's proposal for a program of catastrophic insurance for all federal employees, with the government paying all the premium, came up against strong opposition from the nonprofit plans and some labor spokesmen. They argued that basic coverage should come first. Accordingly, the administration bill failed to pass. Then, committee chairman Tom Murray directed the accounting office to make a study of the feasibility and probable cost of a basic plan with payroll deductions.

Early in September, 11 commercial and nonprofit plans were asked to submit informations on what would be required of federal agencies in administering a basic health program. The GAO then drafted criteria based on this data and submitted them to the agencies. Chairman Murray has set Dec. 31 as the deadline for a committee report on a basic program. Before submitting its plan for catastrophic coverage to the last Congress, the administration had sought an agreement among various insurers on basic coverage for federal workers without payroll deductions, but it was abandoned when no agreement could be reached.

CENTER FOR RESEARCH ON AGING

To encourage and finance research in the mechanisms involved in aging, the Public Health Service has established a Center for Research on Aging, under the direction of the National Institutes of Health. Dr. G. Halsey Hunt, presently associated chief of the PHS Bureau of Medical Services, will head the new center as of Nov. 19. Coordinating all activities in this field in the office of Surgeon General Burney will be Dr. John W. Porterfield, recently named as assistant to Dr. Burney.

The PHS objective is to assist universities and other research institutions in setting up broad research programs. One of the initial steps will be to encourage nonfederal organizations to establish comprehensive research centers on aging, which will be aided financially by the National Institutes of Health. For several years a Federal Council on Aging has attempted to coordinate research in this field.

In describing the new center, Secretary Folsom said: "I am hopeful that this new effort will help bring answers to some of the most critical and challenging health problems of our times. There are more than 12,000,000 people in this country today who are over the age of 65; by 1970, there will be more than 18,000,000. Many of our older citizens have special health problems. It is important that more be done to help these problems—to help older persons to greater independence and self-sufficiency and a life more free of disease and disability."

REHABILITATION PROBLEMS

The federal-state partnership in solving medical and rehabilitation problems was emphasized repeatedly during the four-day annual meeting in Washington of the National Society for Crippled Children and Adults. This theme was underscored during a panel discussion of officials of the Department of Health, Education, and Welfare and the Public Health Service. Presiding over this panel was Dr. Elmer Hess, immediate past-president of the American Medical Association. Dr. Leroy E. Burney, PHS surgeon general, warned against the "isolated or exclusive approach" to solving health problems in communities and states. No one profession or group can do the job alone, he said. Accordingly, the PHS and HEW strongly favor the partnership method. Dr. Burney also noted there were "shortages in all types of health personnel," but he was confident some of the health bills passed by the last Congress would alleviate the situation.

Dr. Martha Eliot, chief of the Children's Bureau, cited an accelerated trend toward an integrated medical and educational approach in treating crippled children. She placed in this category cerebral palsy, sight conservation, cleft palate, hearing impairment, congenital heart disease, epilepsy, and orthodontic defects. "If we are to do the maximum job of rehabilitation for children and adults, we must somehow weave our medical and orthopedic clinics, our sheltered workshops, our dental clinics, or mental health clinics, our vocational rehabilitation and educational services into a coordinated and integrated program. We must see that they merge into a smooth-flowing rehabilitation program for our handicapped citizens, adults and children alike," Dr. Eliot declared. Mary E. Switzer, head of the Office of Vocational Rehabilitation, said the HEW "approaches the problem of disability as a challenge to our ingenuity, our courage and our willingness to see a difficult problem through."

AEC RESEARCH GRANTS

Among recent research grants by the Atomic Energy Commission were 22 awards, totaling $354,400, to medical institutions. The contracts are part of the AEC's program to assist research and development in fields related to atomic energy. The University of Michigan received the largest award ($20,000) of the three new contracts in the medical sciences. It will be used for studies with an x-ray monochromator and

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From the Washington Office of the American Medical Association.

x-ray irradiation service operation. New York University's Bellevue Medical Center was granted $18,975 for research in the distribution and persistence of radioactive aerosols in the lungs of animals. An award of $10,000 will be used by Wayne University to study the effects of maternally administered phosphorus-32 on fetal and postnatal development of the rat. The AEC renewed 19 medical basic science contracts, totaling $305,425, the largest, $50,000, going to the University of Michigan.

RUSSIAN MEDICAL RESEARCH

A new program to keep American scientists up-to-date on Russian medical research findings has been started by the National Institutes of Health, using $250,000 appropriated by the last Congress. Soviet scientific information in the biological and medical sciences will be translated and distributed. Initially two Soviet medical journals, *The Soviet Medical Reference Review*, and a limited number of monographs will be reprinted in English and distributed to medical and scientific libraries, and to government agencies. These reprints will also be available for purchase. Plans are being made for the publication of a Russian-English medical dictionary and a directory of Soviet medical and biological research institutes. The National Science Foundation conducts a similar program in physical sciences.

PUBLIC SAFETY IN THE NUCLEAR INDUSTRY

Atomic Energy Commission official concerned the insurance aspects of radiation hazards has led out the government's position on public safety in the nuclear industry. W. J. Satterfield Jr., chief of the AEC insurance section, said the ultimate safety of the public is dependent on a program that (1) makes an extremely careful and detailed evaluation of every nuclear reactor to assure that all possible hazards have been recognized and defined; (2) assures that all reasonable steps are taken to minimize the probability of the occurrence of an accident; (3) relies heavily on the technical competence of the designers and operators of the reactor and of those making the hazard evaluation, and on the administrative and management abilities of the operating group; and (4) continually checks on the activities of the reactor operator for compliance with the rules of the AEC and the conditions of the license.

The official said one of the most difficult problems is the ultimate disposal or "actual return to nature" of radioactive wastes. Storage, he said, is expensive and in itself is a possible hazard. "On the other hand, unless the waste material is returned to nature in certain specific ways the natural physical, chemical and biological phenomena may conceivably result in undesirable situations. The AEC is currently sponsoring research and development of better waste handling methods at many sites." He cited these figures on the safety record in the federal atomic energy program from 1943 to 1955: out of 184 fatal accidents in over 2,500,000 manhours of work, only 2 were from radiation and those had nothing to do with reactor operation.

WORKSHOP IN ANESTHESIOLOGY

The first national postgraduate workshop in anesthesiology will be held at Walter Reed Army Medical Center in November. About 50 Army nurses will discuss the educational, professional, and personnel aspects of anesthesiology. . . . The federal hospital officials are now meeting at the 13th Interagency Institute for Federal Hospital Administrators at the Walter Reed Center. The latest management methods and techniques in administration providing better patient care are being discussed in the three-week program. . . . The United States Air Force has announced that 180 of its physicians have started residency training and 155 are in internships. Approximately two-thirds of the latter will be trained in civilian hospitals. . . . The Army has issued a new brochure on its Medical Intern Program. The pamphlet, designed to bring young graduate doctors into the program, lists the qualifications necessary for acceptance and discusses the facilities of the eight hospitals where the program is in operation.

MISCELLANY

Under the Professional Nurse Traineeship Program of the Public Health Service, 650-to-700 graduate nurses will be assisted in further education this year. Nearly 2 million dollars have been granted to 56 schools of nursing and public health. . . . The newest member of the National Advisory Cancer Council is Dr. J. F. Ross, associate dean of the school of medicine, University of California. The council, which advises on research activities of the National Cancer Institute, has 12 members—6 leaders in science and 6 leaders in education and public affairs. . . . The Food and Drug Administration announces that tranquilizing drugs for use in animals will be restricted to professional veterinary use to prevent possible unsafe diversion to human use. . . . The FDA seized seven shipments of drugs last month because the potency was not stated on the labels and five shipments because of false labels.

Intraperitoneal Air.—The finding of free intraperitoneal air on the roentgenogram has come to be considered a sign of a perforated gastrointestinal tract. Not only practicing physicians but textbook authors, as well, consider free subdiaphragmatic air as pathognomonic of perforated peptic ulcer. Undoubtedly, perforated peptic ulcer is the most frequent cause of free intraperitoneal air in patients with abdominal complaints, but a number of other, often recognized, conditions also present this roentgen finding. Some occur frequently, some rarely, but each is of sufficient importance to be thought of by the radiologist. . . . The most frequent artificial introduction of air into the abdomen occurs at the time of abdominal surgery. The presence, but not the duration, of air under the diaphragms may be predicted whenever the abdomen is surgically explored. Most investigators estimate the maximum persistence of air as being two to three weeks, but one observer extends this period to from four to six weeks. A full therapeutic pneumoperitoneum has been known to take eight weeks for absorption, so this latter figure is not unreasonable, particularly in view of an abnormal peritoneal surface. In the first few weeks postoperatively, free air alone cannot be considered evidence of perforation or reperforation of an ulcer, leakage of a suture line, or intestinal necrosis. The decision to reexplore the abdomen will rest on clinical evaluation, not on the unsupported roentgenologic finding.—H. W. Fischer, M.D., Free Intraperitoneal Air, *The American Journal of Roentgenology, Radium Therapy, and Nuclear Medicine*, July, 1956.

THE JOURNAL

of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 162, NO. 11 CHICAGO, ILLINOIS NOVEMBER 10, 1956

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HEALTH HABITS AND HEART DISEASE—CHALLENGE IN PREVENTIVE MEDICINE

Edward P. Luongo, M.D., Los Angeles

• *A comparison of health habits has been made between a test group of 100 patients with manifest coronary disease and a contratest group of 200 people with the same distribution of ages and occupations but without coronary disease. The importance of dietary habits is illustrated by the finding that only 27% of the test patients had average diets with a variety of food and an apparent balance between caloric intake and energy output, while 60% of the contratest group had a satisfactory nutritional status. The exercise patterns differed significantly also, with 70% of the test group showing no regular exercise patterns either at work or away from it, as compared with 30% of the contratest group. No influence of tobacco or of alcohol was evident in this study, but, among the patients who survived a coronary attack, 71% have been using alcohol in moderation anywhere from 1 to 10 years since the attack, and in this group all claim beneficial effects with less anxiety. Stress patterns were found to be important, but occupational titles were not reliable as indicators of occupational stress. Preventive measures should be taken if the heart rate and diastolic pressure show a sustained rise, regardless of electrocardiographic findings, and such measures become urgent if there is hypercholesteremia, xanthomatosis, or diabetes. There is evidence that the real culprits in coronary disease are not hard work, overexercise, or occupational stress but sedentary living and poor health habits.*

Many leading cardiologists[1] believe that health habits, including nutrition and exercise patterns, are important factors in the prevention and postponement of coronary disease. This opinion received further support from preliminary observations in a study of 100 proved cases of manifested coronary disease compared with 200 control cases of patients in the same age group. The cases studied included anterior myocardial infarctions (42.5%), posterior myocardial infarctions (37.5%), angina pectoris (16.25%), and myocardial insufficiency (3.75%). These were compared with a control group of patients with no clinically manifested coronary disease, with approximately the same occupational distribution. All patients in each group were in the fourth or fifth decade of life. There was one female in the group with coronary disease and none in the control group. Clinical diagnoses in the coronary group were confirmed by at least one and in many instances two cardiologists. Many of the patients were studied further after recovery from the attack by the work classification unit of the Los Angeles County Heart Association. Cases in the study represent 100 out of approximately 160 known cases that have occurred in an employee population of 6,000 over a 10-year period. Of those coronary patients surviving (82%), 50% returned to their regular occupations and the rest to limited duty jobs. About one-half of these employees have been working 6 to 10 years since their attacks.

Nutrition

The study suggests strongly the role played by total caloric intake as a factor in the problem of prevention and postponement of coronary disease. Dr. Frederick Stare has stated that "nutrition is the most important environmental factor affecting the health of our population today."[2] Since 1948 I have been part of a preventive industrial medical group that has emphasized the importance of control of obesity and overweight among all our employees. In the majority of cases of overweight patients we have stressed the need for regular, moderate exercise as an important aspect of weight reduction. We feel also the most practical advice to employees is to "cut down" and not "cut out" foods. Bathroom scales at home and weighing scales available in the medical department have proved valuable psychological adjuncts to this program. Rapid eating is advised against in counseling overweight employees, since this interferes with adequate rise in blood sugar level, which in turn controls the appetite through the hypothalamus in the brain. Many rapid eaters have poor dental hygiene; they believe that the sooner they can finish masticating food the better, and, as a result, they gulp food rapidly. Dental hygiene, therefore, is a factor in weight control. By these

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Chairman's address, read before the Section on Preventive and Industrial Medicine and Public Health at the 105th Annual Meeting of the American Medical Association, Chicago, June 13, 1956.

simple methods we have been able to reduce the incidence of overweight from 25% of the employee population in 1951 to 15% in 1955.

In the medical histories of those cases of manifested coronary disease studied, in more than two-thirds of the cases the total caloric intake was more than that necessary for the energy expended either on or off the job. More than two-thirds of the patients with coronary disease were overweight or obese on the average of 10 to 15 years prior to the attack, while in the control group of the same age range, only one-third were obese or overweight 10 to 15 years prior to this study. Only 27% of the patients with coronary disease had average diets with a variety of food, and in these apparently there was a balance between the total caloric intake and energy expended. These individuals had been able to maintain average or ideal weight 10 to 15 years prior to attack. By comparison, in the control group 60% of the patients had had average diets with maintenance of weight at average or ideal levels 10 to 15 years prior to the study.

Exercise

There was a close correlation between overweight, excessive total caloric intake, and lack of exercise patterns in the coronary group, with 70% showing no regular exercise patterns either at work or away from the job. Approximately the same percentage of patients were overweight due to excessive total caloric intakes. In contrast, only 30% of the control patients had no regular exercise patterns, and the records of these patients show the same correlation as to overweight and lack of exercise. These findings tend to support the present concept that exercise is an important aspect of weight control, and the lack of it, along with other factors, may cause predisposition to coronary disease.

Tobacco

Since the introduction of tobacco into Europe, soon after the discovery of America, its relationship to health and morals has been a controversial subject. In spite of various denunciations through the centuries by medical men, churchmen, and others, the smoking of tobacco continues to enthrall a considerable proportion of people in our culture. To date there is no convincing evidence in the literature that smoking of tobacco has any effect in accelerating sclerosis or in producing coronary disease.[3] In this study we found the consumption of tobacco was approximately equal in the coronary and the control cases, with 18% nonsmokers (mostly lifetime) in both groups. The rest (82%) in both groups consumed between one and one and one-half packages of cigarettes per day for a period of 10 to 15 years prior to attack or prior to this study. This would lend some support to the concept that tobacco is a nonetiological factor in coronary disease. It does not mean, however, that tobacco is without possible harmful or embarrassing effects on already diseased coronary arteries or, for that matter, on already diseased peripheral arteries.

Alcohol

As in the case of tobacco, the consumption of alcohol seems to have little or no relationship to the production of coronary sclerosis. The percentage distribution of those patients who did not use alcoholic beverages in any form was about the same (10%) for the coronary and the control group. In those patients who survived attack (82%), 71% have been using alcohol in moderation anywhere from 1 to 10 years since the attack. In this group all claim beneficial effects, with less anxiety. While one cannot relate any beneficial effects of alcohol directly to improved coronary blood flow,[4] there is evidence in the literature that in moderation alcohol may diminish the work load of the heart by reducing the pressure in the small peripheral arteries of the body. More important, alcohol in moderation may relieve anxiety through cerebral action. This anxiety frequently contributes to the onset of heart pain.

Occupation

Different occupations with different physical, emotional, and mental demands have been suspected as etiological factors in producing coronary disease.[5] The only conclusive effects seem to lie in the individual employee's health habits, including nutrition and exercise, and do not depend on job titles per se. If employees in sedentary occupations have poor health habits and do not have good exercise patterns, they may be expected to be more prone to coronary disease than employees whose work requires regular exercise and whose health habits, including nutrition, are good. In this study the occupational distribution of cases of coronary disease was approximately the same as the occupational distribution in the control group, taking into consideration the percentage occupational make-up of the total employee population. The incidence of manifested coronary disease was the same among executives, professional, clerical, and skilled workers, all doing moderate or sedentary work. The incidence among unskilled workers performing arduous work was lower compared to the other occupational groups. Occupational titles are unreliable from the standpoint of correlating epidemiological data with any conclusive effects of occupation. Further, in any true evaluation of these effects, we must be just as concerned with what an employee does away from the job as what he does on the job. I believe we can be certain that there is no evidence that physical exercise at work or play causes coronary disease.

Occupational and Nonoccupational Stress

Stress due to fears, phobias, frustration, anxiety, and fatigue certainly should be listed in the category of health habits, and its appraisal is an important part of any physical examination. Whether we consider stress, in the light of Cannon's theory of emergency epinephrine release, as a causative factor in heart disease or whether we consider stress as an expression of hormonal imbalance in the individual, we know that one of its frequent results is overeating. Individuals subject to nervous tensions, with feelings of frustration and suppressed hostility, at either an occupational, social, or domestic level, frequently find food, in nibbles or at a banquet, a relief from nervous tension. Stress, therefore, insofar as it causes overeating and overweight and affects the individual's outlook on healthful pursuits in life, must remain suspect in the etiological picture of coronary disease. In this study, obvious detectable stress patterns existed in most of the patients with coronary disease prior to the attack. These precoronary stress patterns were related more to cultural, domestic, and social problems than to the occupation. They were distributed over all occupational categories, with only a small preponderance in the executive group over the nonexecutive group. In the control group obvious detectable stress was about equal among clerical, professional, and skilled workers (30%) and lower among executives and unskilled workers (15%). Whereas 15% to 30% of the control group showed definite stress patterns, about 60% of all the patients with coronary disease had these patterns prior to attack.

Diagnostic Criteria Related to Prevention

Some comment is in order here on the reliability of of our present criteria and diagnostic techniques in determining the existence of diagnosable coronary disease and "nondiagnosable coronary disease" and determining presumptive evidence of candidacy for coronary disease. No doubt improved training of physicians and improved diagnostic techniques have brought about earlier and greater recognition of this condition in patients. We still have too many cases of patients with normal hearts who are on "the psychological scrap-heap" whose only indication of disease is that shown by the electrocardiogram. There is an inherent temptation for the medical profession, and for the public, to rely too much on some mechanical device, such as an electrocardiograph, not only in cardiovascular disease but in other diseases. At the other extreme, we have individuals with strong presumptive evidence of coronary disease who have been "ponounced perfect" on the basis of one electrocardiogram, frequently without the benefit of an exercise tolerance test. In the middle, we have the patients with clinically proved disease and a large number of younger candidates for the disease with only subtle subclinical findings that too often are disregarded.

Our increased knowledge of the disease has made little difference in the prevention of the disease among these candidates.[6] In this connection, waiting for presumptive evidence of the disease on the electrocardiogram often is too late. In our study, among those patients with coronary disease who had two or more electrocardiograms within six months to two years prior to attack, 50% had normal findings. In the control group 68% had two or more normal electrocardiograms six months to two years prior to this study. Thirteen percent had abnormal electrocardiograms with T-wave abnormalities and "nonspecific" changes.

Progressive Rise in Pulse Rate and Diastolic Pressure

We were able to observe some interesting correlations regarding pulse and diastolic pressure changes in the two groups over periods of 10 to 15 years. Over two-thirds of the patients with coronary disease showed a sustained rise in pulse rate (15 to 30 beats per minute) and diastolic pressure (10 to 30 mm. Hg) on the average of two to five years prior to attack. By contrast, only one-third of the control patients showed significant changes in pulse rate or diastolic pressure two to five years prior to this study. Preliminary observations suggest that these pulse and diastolic (with or without systolic changes) pressure elevations, correlated with findings on nutrition, stress, and sedentary habits, are important presumptive evidence of candidacy for coronary disease, and patients in this category should be treated as such by proper preventive measures, regardless of electrocardiographic findings. Preventive measures are even more urgent when these patients also show evidence of hypercholesteremia, xanthomatosis, and diabetes. In this study, 37% of the patients with coronary disease showed evidence of metabolic disorders as compared to 14% in the control group.

Obviously some of the patients in the control group are candidates for coronary disease at a later date, even if proper preventive measures are taken. However, we hope that these cases can be prevented, limited, or postponed as long as possible. This in effect is the challenge to all of us in preventive medicine, whether we be in public health, aviation medicine, or occupational medicine; whether we be in general or specialized medicine; or whether we be teachers.

Comment

There is evidence that sedentary living and poor health habits are the real culprits in coronary disease and not hard work, overexercise, or occupational stress. The disease incidence does not appear to be governed by occupational titles but more by what exercise an individual gets on or off the job and what his nutritional status has been 10 or 15 years prior to his fourth or fifth decade in life. It appears that insofar as proper health habits (including nutrition and exercise) are concerned, individuals should start training for middle and old age during their youth or childhood. Equally important, every individual should carry on these patterns of nutrition and exercise, within the realm of common sense, as long as possible in middle and old age. This may be difficult because of stresses, cultural problems, and economic situations later in life.

Preliminary findings of the study suggest the importance of appraisal of health habits as an integral part of every examination, in both industrial and private practice. Also, they reemphasize the importance of regular periodic examinations as a means of limiting and postponing the number of cases of coronary disease occurring prematurely in patients in the fourth decade of life. Physicians, in the future, will need more scientific and systematized information on positive health measures as they relate to normal nutrition and the tailoring of individual exercise patterns. Also, in order to prevent or postpone coronary disease, physicians must have time in their offices to appraise life interests and cultural pursuits of patients for whom they are responsible.

This study and others are reemphasizing the need for continuing research on nutrition as it relates to chemopathology and molecular disease. In this connection we have no positive criteria for prescribing diets for the prevention of atherosclerosis. While the work being done on the relationship of fatty acids to blood lipids[7] seems to open up avenues for research that may be productive of certain criteria, we find that the safest and most practical dietary advice is to "cut down" and not "cut out" and to encourage a variety of food in the diet with a restriction on unwarranted or excessive use of total fat. This would not apply, of course, to those with excessive amounts of cholesterol in their blood. To our best knowledge today, these candidates for coronary disease should become vegetarians.

Presumptive evidence in the form of abnormalities on the electrocardiogram usually comes too late for effective preventive measures. Progressive elevation in pulse rate and diastolic pressure in overweight men in the fourth and fifth decade of life is probably as good a criterion as the electrocardiogram for instituting preventive measures related to health habits.

Conclusions

It is hoped that this preliminary report will assist in the stimulation of other epidemiological studies on heart disease, in both private industry and other organizations where sufficient data are available. We will continue to obtain epidemiological data on present and future known cases. We and our predecessors in preventive medicine accepted the challenge of controlling morbidity and mortality due to infectious diseases. Our successful effort in this field has added to the longevity of man's existence on this earth. We have more men and women reaching middle and old age when coronary and other degenerative diseases are more prevalent.

We can add further longevity and, more important, breadth and depth to man's existence by thinking more in terms of positive health measures and by inculcating into our philosophy of medicine a new definition of health—one that is independent of the word disease and one that stresses good physical and mental health habits early in life that can be productive of better mental and physical efficiency in middle and old age. We must exert a continual alertness for new cultural problems with new habits, excesses, deficiencies, stresses, and strains that can rob us of our victory over the infectious diseases by taking lives of those recently saved from curable and preventable infectious diseases.

Everywhere the wonder of technicological advances goes, striking shackles from 100 men at each step and making mechanical horsepower and brain power cheaper than the humblest brawn. More and more men will be freed of certain distasteful and obnoxious labor and will have more time and money for leisure. Will this leisure be productive of a fuller life with more positive health? Already we have evidence that coronary disease in a sense is a "disease of prosperity," having no respect for any social or occupational class.[8] Here is our modern challenge. We in medicine as part of a creative minority can meet this challenge. We can do this if we discard outdated notions of what is health and what is disease. If we can guide men in the intelligent use of their abilities, resources, stamina, and interests in life, we can help them lead satisfying and happy existences.[9] If we as part of a creative minority fail, we will find ourselves part of a civilization unprepared for the economic riches it fought so hard to obtain.

612 S. Flower St. (54).

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DIVIDING LINES IN SPECIALIZED MEDICAL PRACTICE

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• *There are no rigid dividing lines in medical practice to which a physician is compelled to conform. The American boards, while limiting the practice of their diplomates, do not actually specify the boundary of limitations. Training and dexterity should be the basis for the doctor setting his own perimeter of practice. Dermatological practice provides perhaps the best example of the lack of dividing lines in its relationship to all the other fields of medicine.*

Practically as old as civilization itself is the phenomenon of specialization, by which certain individuals limit their activities to a small segment of the sphere of human endeavor in order that they may thereby be able to acquire a more thoroughly encompassing knowledge and a greater degree of skill. Even when the sum of all the facts previously learned by the race was yet small there was a surprising variety of occupations, each of which attracted its share of practitioners by presenting an opportunity for them to exploit advantageously certain of their own physical or mental attributes, such as those of size, strength, acuity of one or more of the senses, dexterity, or intelligence. The dividing lines between such specialties were thus quite naturally rather sharply delineated, since each demanded that an apprentice must possess a certain set of inherent attributes if he were to succeed. Because of this sort of natural, automatic selection, specialization has almost always been beneficial to humanity, and its influence has been responsible for an overwhelming proportion of all progress.

In medicine, the earliest historical records reveal that specialization had already developed to a considerable degree. No more than a brief glance back-

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Chairman's address, read before the Section on Dermatology at the 105th Annual Meeting of the American Medical Association, Chicago, June 13, 1956.

ward through the centuries will prove that it is incorrect to refer to our own times smugly as "the age of specialization." Studying bones recovered from early Stone Age strata, LeBaron found the skeletons of 18 men who had had fractured limbs, only 3 of which would be considered to have healed poorly, even by today's standards, thereby indicating that there were persons then living who had become expert at setting fractures. According to Herodotus, there were in early Egypt special physicians for every part of the body. One of the earliest of the Egyptian papyri, dated about 2000 B. C. was devoted to disease of women, and another, concerned exclusively with surgery, appeared about 1600 B. C. Imhotep became famous for his ability to cause people who were in pain to be able to sleep, thus probably deserving to be called the first anesthetist. The greater part of Aesculapius' fame was as a military surgeon. Today, a Hippocrates would probably be called an internist especially adept at differential diagnosis, while a Galen would be sought after as one best able to select and guide therapy.

However, the dividing lines between these medical specialties were not as sharply drawn as in other fields of human endeavor. In today's vernacular, the ancient men of medicine would all be classed as general practitioners, some of them giving "special attention" to a particular field. Indeed, it is difficult to see any of the reasons why they elected to narrow their practices at all, beyond the fact that an appealing opportunity to do so must have appeared at an appropriate time.

It is equally difficult to discuss the boundaries of the medical specialties as they exist today, or the reasons why an individual selects one as his life's work in preference to the others or to an unlimited form of practice. It must be granted that there are certain phases of medicine in which great physical strength and stamina are useful assets to the operator, some which demand of him a greater than average degree of emotional imperturbability and some in which exceptional dexterity is an advantage; but, in general, anyone capable of becoming a practitioner of medicine at all could probably succeed as a specialist, if the desire and the opportunity were present at the proper time.

It is probably correct to state that even today there are no rigid boundaries whatever to any of the medical specialties. Each practitioner apparently guides himself according to his own interpretation, insofar as he is permitted to do so by his conscience and by the pressures brought to bear upon him in his own locality by others who practice his specialty and by his competitors in other fields. Even in different geographical areas of the United States there are wide variations in these boundaries. Each of the American boards in the various specialties requires its diplomates to "limit their practice" to that respective field, but nowhere are these boundaries specified by these organizations themselves. Thus, no specialist knows exactly what his limitations are supposed to be.

It is at this point that I must emerge as a partisan and, henceforth, speak as a dermatologist, for I believe that there are several reasons why it is singularly appropriate for a dermatologist to present this subject, not because he is capable of being less prejudiced, but on the contrary because he cannot avoid being biased in every conceivable direction. This is caused by the fact that dermatology is unique among the specialties in relationship to all dividing lines. Every other specialty has one or more of the segments of medical practice that it is undisputedly permitted by all other specialties to call its own. For example, no one but a highly qualified ophthalmologist attempts to remove cataracts or to graft corneas; all such cases are gladly conceded to him. Fenestration operations belong exclusively to otologists and cases of brain tumors to neurosurgeons, but even the most complicated of dermatological techniques is considered by the nondermatologist to be either entirely unnecessary or so simple as to be within his reach the first time he attempts it. Conversely, no specialty other than dermatology can say that its field is encroached upon in at least some degree by every other specialty. As an illustration, it would almost certainly be impossible to discover any practitioner of medicine who could honestly say that he had never once in his career attempted to treat a skin disorder.

Mechanisms Utilized in Dividing Medicine into Specialties

To a large extent the overlapping between specialties is due to the fact that in dividing up the ailments that can afflict the human body there is much disagreement as to which of several entirely different sets of rules should govern. For example, one method of division is based upon the belief that each specialty should concern itself exclusively with a certain area of the body; another places its emphasis almost entirely upon different forms of treatment; and a third considers the type of disease of paramount importance.

The first group of specialties named aboved may be termed "topographic," "regional," or, perhaps, "organic." Practitioners of one of these specialties limit their activities to the care of abnormalities involving only a certain area of the body, a certain organ, or a certain group of allied organs. By such a limitation, they consider themselves able to become expertly acquainted with all of the disorders that may be encountered in that region, rare as well as common, and to differentiate between them. They also claim to have mastered all of the methods by which these conditions should be treated, including the techniques involved in the use of whatever mechanical or electrical appliances may be required. Several of these specialties may be said to be "complete," because within the selected area both the medical and surgical aspects are covered. This group includes dermatology, urology, orthopedics, gynecology, proctology, ophthalmology, otology, and rhinolaryngology. Perhaps dentistry should be included here. There are other specialties, which we may class comparatively as "incomplete," whose perimeters are determined similarly by topography, except that in each instance there is a sharp division into two subsections, one surgical and the other medical. Here are included such pairs as neurology and neurosurgery, cardiology and heart surgery, pulmonary diseases and chest surgery, and gastroenterology and abdominal surgery.

In searching for an analogous mechanism of division in other fields of human endeavor, it appears that this method of grouping resembles somewhat that of the

Congress of Industrial Organizations among the labor unions in America, in which one of the important criteria for being included in membership is where the work is to be performed. For example, all persons employed in a certain locality, as in an automobile factory, are members of an automobile workers' union, regardless of the type of work each individual performs or the tools he uses. In the parlance of the labor unions, this is termed a horizontal type of organization. The analogy is not entirely correct, for there is a much higher degree of specialization among the workers within such a group than is found in the corresponding type of medical organization.

Based upon an entirely different concept is the mechanism of division in the second large group of medical specialties, in which the supremely important factor is considered to be the ability to use expertly a certain tool or class of tools or to administer a particular type of treatment, without regard to the region of the body involved or the kind of disease present. In this category are experts such as surgeons with scalpel and suture, radiologists with various forms of radiant energy, pathologists with laboratory apparatus, and physical therapists with their several modalities. Here there is a clear analogy with the craft guilds of the American Federation of Labor, represented by experts such as carpenters with saw, plane, and hammer; plumbers with die and wrench; machinists with lathe, drill, and mill; and musicians with various musical instruments. These pursue their particular crafts in whatever locality they may be required. Again using the vernacular of the labor unions, this mode of division is termed vertical.

The third group of medical specialties is delineated by placing the emphasis upon the type of disease that is presented, without regard to its topographic location or the sort of therapy that it demands. Here the best all-inclusive example is the oncologist, who claims ability to treat neoplasms without regard to where they may occur or with whatever modality is indicated, including surgery, radiation, or medication. There are a number of subgroups in this category, classed as less complete because the related surgery or radiation is not included in their respective fields, such as internists, epidemiologists, hematologists, allergists, endocrinologists, venereologists, and toxicologists. The analogous situation in nonmedical occupations is represented to a fair degree by such groups as policemen, firemen, Red Cross personnel, and, perhaps, termite-control specialists. An adjective bearing a geographical significance comparable to horizontal or vertical has not been applied here to my knowledge; perhaps the term "diagonal" is serviceable.

There are yet other medical specialties that are not suited to classification in either of these groups previously mentioned, such as psychiatrists, aeromedical personnel, and medical examiners for corporations or insurance companies. It is interesting to note a mode of division in medicine that depends entirely upon the age of the patients (pediatrics and geriatrics), which has no counterpart in labor unions unless it be to such classes as schoolteachers. Perhaps this method can be classed as representing a diagonal in yet another direction.

Divisions of Medicine as Observed in Actual Practice

It might appear that dermatology, being one of the topographic specialties delineated above, should not find itself in disagreement as to boundaries with the other members of that same group. This is not the case, for, as has been already pointed out, the boundaries of dermatology are encroached upon by all other specialties and it in turn encroaches upon each of them.

As an example, consider the boundary between dermatology and proctology. To the dermatologist there appears to be only one logical line of demarcation that needs to be considered, the mucocutaneous junction at the anus. It cannot be denied that from this point outward all that which is encountered upon the surface of the body is skin, subject to all of the diseases to which the skin in general is susceptible, in addition to a few that are peculiar to that area. Thus, it seems to the dermatologist that a physician must of necessity know the greater portion of the science of dermatology, if he is to claim the expertness expected of a specialist in assuming the care of an ailment external to the mucocutaneous junction. Yet some proctologists consider a circular area perhaps up to a dozen inches in diameter centered about the anus to lie well within their field. Dermatologists highly respect the ability possessed by proctologists to deal successfully with such conditions as carcinoma of the colon, fistula in ano, hemorrhoids, and prolapse, all of which require much specialized training and experience. It can be said with confidence that no one certified in dermatology attempts to treat such proctologic conditions. Realizing the importance of acquiring and maintaining skill in such valuable techniques, proctologists naturally devote all of their study time to them and are never found in attendance at skin clinics. Thus, they have no opportunity to learn to respect the difficulties of dermatology. As one example of the resulting lack of diagnostic ability, proctologic literature contains many discussions devoted to pruritus ani. It is obvious to the dermatologist that pruritus ani is not a disease and that it does not even deserve to be classed as a diagnosis, since it is only the translation into Latin of the symptom complained of by the patient. It is also obvious to the dermatologist that there can never be a single, truly successful treatment for pruritus ani, since there are altogether too many different causes that must be differentiated and specifically controlled. Proctologists treat many of these cases on the assumption that they are due to fungous infections, yet never bother to ascertain whether fungi are present. Dermatologists treat itching of the anal area only if there is a dermatosis visible that matches the symptom; otherwise consultation with a proctologist is advised. This is also their procedure when such itching does not subside quickly and simultaneously with the clearing of the dermatosis, since they realize that a deep-seated disease may easily have been the original cause of such a complaint. Dermatoligsts are firmly convinced that it would be better for such patients if proctologists would reciprocate by displaying a similar respect for dermatology.

Lest I be accused of inappropriately singling out proctologists for criticism, I hasten to add that each of the other topographic specialties has similarly included in its field a segment of the surrounding skin.

The skin of the perineum, groins, and pubic area, as well as that of a large part of the abdomen and thighs, is persistently treated by gynecologists and obstetricians. Except for cartilage, which is only infrequently susceptible to disease, the entire external ear is nothing but skin and the surrounding area is strictly a dermatological problem. Even the auricular canal is composed of modified skin. Yet some otologists still treat many cases daily of what they class by inspection alone as "fungous infections," even though it has long been known that fungi seldom cause disease in this area. Large areas of the skin surrounding the nose, mouth, and eyes are similarly included in the fields of endeavor of some rhinologists, laryngologists, and ophthalmologists. Many orthopedists customarily assume the care of the cutaneous surface of arms, hands, legs, and feet and internists that of the trunk. None of these practitioners devote any appreciable time to becoming acquainted with dermatological diagnosis or therapy.

With those groups that advocate dividing medical practice strictly according to the classes of tools that are to be used in the treatment of disease, the dermatologists have even more profound disagreements as to dividing lines. Perhaps the best example concerns the radiologists who frequently, and sometimes quite vociferously, express the opinion that dermatologists are straying inappropriately outside of their field by possessing and utilizing in their offices apparatus for the production of roentgen rays. In refutation, it is first necessary to point out that all of the early pioneers in roentgen therapy of the skin were dermatologists, and this science has been continuously studied and advanced almost exclusively by them ever since. Also, it seems obvious to the dermatologist that in order to treat a skin disease properly with whatever modality may be chosen, the diagnosis must first be ascertained, a procedure for which the roentgenologist is seldom if ever trained beyond the level of an intern. Even if the diagnosis is clear and x-ray therapy is actually indicated, the roentgenologist is unlikely to be able to bring a greater degree of skill to bear upon the administration of the therapy than the dermatologist, who devotes much more study time and practice to the roentgenologic aspects of strictly dermatological therapy. Furthermore, the dermatologists' x-ray machines are constructed especially for treatment of the skin and function better in that field than the all-purpose apparatus of the roentgenologist.

In spite of the high degree of ability to differentiate between tumors of the skin, that dermatologists acquire by intensive study, experience, and constant practice, their habit of subjecting every lesion to biopsy makes them aware of the inaccuracy of attempting such differentiation by visual means alone. Such histopathological study not only serves to distinguish between malignant and nonmalignant lesions but reveals a wide range of different types and degrees of malignancy, without which knowledge it is impossible to select the best therapy. Radiologists frequently administer x-ray therapy to lesions that they class as cancer by inspection alone and are later able to boast of high rates of cure by virtue of the fact that a large proportion of such lesions were in fact benign.

Wherever special clinics exist devoted to cancer, attended by specialists in all fields, it always becomes evident that certain cases are better treated by one modality than by another. From these studies, elaborate criteria have been developed upon which the selection of the therapy should be based. None of this experience is likely to be utilized in certain forms of medical practice, since it is beyond the realm of possibility when dealing with human nature to expect the roentgenologist to refer to the surgeon that half of the patients who come to him with cancer which can best be treated by surgery and expect the same consideration from the surgeon in return. The dermatologist has all methods at hand and is able, therefore, to act impartially, to the patient's benefit.

As to the dividing line between dermatology and surgery, there can be no quarrel with the opinion that no one should attempt any operative procedure that is beyond his training and ability, or which could, because of unexpected findings, lead him beyond his depth. However, it must be seriously questioned whether any surgeon actually believes that a dermatologist is less capable than he of performing the usual small dermatological surgical procedures. At times surgeons carry this view to absurdity by implying that the scalpel should be forbidden to all but fully trained surgeons.

With regard to the specialties devoted to a certain type of disease, a good example is oncology, which has set up its own dividing lines in the field of cancer. Where skin cancer is concerned, these lines are usually drawn to the exclusion of dermatologists. These oncologists claim to be expert in the diagnosis and therapy of neoplasms, without limitation as to the type of growth involved, its location in the human body, or the mode of treatment best suited to its eradication. To fulfill this claim would seem to demand a veritable constellation of superskills, combining clinical and histopathological differential diagnostic ability of the highest degree in all areas of the body, the combined dexterity of all of the other surgical specialties in their most difficult phases as presented by malignancies, and expertness in all types of radiotherapy and the use of drugs. Although it is probable that no one has attained this goal, it seems to me that such a Caesar, having eaten of special meat and grown so great, would find it too much below his dignity to quarrel over common moles and warts or small cutaneous tumors. To do so thereby would admit his inability to attract to his care a number of cases sufficient to keep him busy of the type for which he believes he is so well prepared. Whatever spare time he has would seem to be better spent in maintaining his astounding dexterity in so many directions.

Comment

I hasten to say that all of this encroachment does not dismay nor anger dermatologists nearly as much as might be presumed. They realize that such a large proportion of human illness involves the skin that there is still enough of dermatological practice left, in spite of all of the efforts of other practitioners. It has been said that, if the certified obstetricians were suddenly to be given the exclusive right to deliver all babies, as they frequently suggest would be appropriate, they would scream for help within a week. Similarly, dermatologists know that they could not care for all cases of skin disorders, even by working night and day. They do not resent the competition of other doctors who are able to succeed in rendering good service to patients with dermatological disorders. However, they see many examples of the harmful results of injudicious treatment, and from time to time they voice a warning.

Dermatological techniques in general lack the spectacular and obviously difficult facets possessed by certain phases of other specialties. Yet dermatology appears easy only to one who has not yet begun to study it. Having spent nine years in the general practice of medicine before beginning to specialize, I consider myself qualified to state that differential diagnosis and therapy in many phases of dermatology are at least as difficult as in any other branch of medicine, and no day passes without my reflecting wistfully that some other specialty would be easier. Dermatologists cannot understand how anyone who does not appreciate these difficulties and prepare to meet them by intensive study can hope to succeed in treating all diseases of the skin.

This paper is not intended to suggest that the perimeters of dermatology should be expanded. Dermatologists believe that the only appropriate boundaries are those that have always existed, rigidly established by the manner in which nature has for eons distributed skin over the human body. They are also satisfied with the way in which these perimeters have become accepted throughout the years by a large and growing proportion of the population and of the medical profession in general, which holds that complicated skin disorders of all kinds are best diagnosed and treated by skin specialists. They do not attempt, however, to force other doctors to conform to this opinion and usually comment on the subject only when it becomes necessary to refute what they consider to be unjustified criticism or to parry attempted interference with their proper functioning. I have tried here only to point out a few of the reasons why dermatologists are not willing to fold their tents and steal away, leaving all of the science of dermatology to be divided piecemeal among the other specialties, where it would always occupy a position of secondary importance and never receive the attention it deserves.

In general, it seems to be entirely proper that there are no rigid dividing lines in medical practice to which any doctor is compelled to conform. Each practitioner must set and observe his own perimeters, in a manner as unbiased as possible, by accepting only those cases for which he knows that his training and dexterity have prepared him to furnish the highest quality of medical care. If there must be dividing lines in medical practice, let them always be designed for the benefit of patients, not of doctors.

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CONTROLLED RESPIRATION DURING CESAREAN SECTION

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• *The condition and behavior of 418 newborn babies were studied after delivery by cesarean section, and comparisons were made according to the type of anesthesia received by the mother. Group 1 consisted of 96 mothers who received spinal anesthesia; group 2, of 165 mothers who received general anesthesia (thiopental sodium, cyclopropane with oxygen, and sufficient dimethyl tubocurarine to maintain a quiet operative field); group 3, of 157 mothers who received thiopental sodium, cyclopropane with oxygen, and enough of either dimethyl tubocurarine or succinylcholine chloride to allow complete manual control of the mother's respiration. Data on the number of minutes elapsing before the baby cried loudly permitted quantitative analysis of the results. The incidence and severity of depression in the babies was found to be least when spinal anesthesia was given. Comparison of groups 2 and 3 showed that manual control of the maternal respiration resulted in much less depression in the infants of group 3 than was seen in the infants of group 2, who were dependent on the spontaneous maternal respiration. When general anesthesia becomes necessary in obstetrics, the plane of anesthesia should be kept as light as possible, the duration of anesthesia should be as brief as good teamwork by obstetrician, anesthesiologist, and nurses will allow, and the mother's respiration should be supplemented by full control of her breathing, so as to ensure the best possible oxygenation with best possible elimination of carbon dioxide for mothers and babies.*

On Jan. 19, 1847, James Simpson administered the first recorded obstetric anesthetic when he gave open-drop ether to a mother during her delivery. Six years later, when John Snow gave chloroform to Queen Victoria during the delivery of Prince Leopold, the popularity of obstetric anesthesia was assured. Obstetrics was thus one of the earliest fields into which the anesthetic art was introduced. In spite of long experience, however, the field of obstetric anesthesia remains highly controversial. The place of general anesthesia in obstetrics, as opposed to regional methods, has long been a subject of debate. General anesthesia has many advantages. It is reliable and convenient. It is safer in the hands of the partially trained administrator.

On strictly scientific grounds, it is easy to condemn the use of general anesthesia in obstetrics because of its adverse effects on the newborn infant. This belief is strongly held in many teaching centers, and those who bear the responsibility of resuscitating asphyxiated babies usually agree. Hingson and Hellman have shown that neonatal mortality is not significantly influenced by the choice of anesthesia.[1] Lund has shown that the mortality rate for normal newborn infants is not greatly altered by different types of anesthesia but that the mortality rate for the premature and the distressed fetus is significantly higher when general

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From the Department of Anesthesiology, Hartford Hospital.
Read before the Section on Anesthesiology at the 105th Annual Meeting of the American Medical Association, Chicago, June 14, 1956.

anesthesia is elected.[2] Evaluations of the mental development of children who were asphyxiated following delivery have been conflicting in their conclusions. Some recent studies have demonstrated little or no adverse results from asphyxia.[3] Although the sequelae of asphyxia may elude present investigative methods, common sense demands that hypoxia following birth be regarded as a hazard.

Selection of Cases

In order to study the depressant effects of anesthesia upon newborn babies, a group of patients has been selected in such a manner that causes of depression other than anesthesia might be eliminated from consideration. Injury and distress to the fetus during labor and delivery have been largely ruled out by selecting for study only babies born by repeat or elective cesarean section. All the infants were born of healthy mothers. None had any significant malformation that could be diagnosed, and all babies weighed 2,495 gm. or more. No twins were included. Premedication was uniformly secobarbital (Seconal), 100 mg. administered two hours before delivery, and atropine, 0.4 mg. one hour before delivery.

This method of selection was employed in order to obtain a group of newborn infants in whom any respiratory depression at birth would most probably be caused by anesthetic agents. Diagnostic techniques are not sensitive enough to reveal all abnormalities, and, no doubt, the criteria of selection were violated in some instances. The number of such abnormalities, however, should be few in number.

Methods of Anesthesia

Three types of anesthesia were administered for the cesarean sections selected for this study. Group 1 included 96 mothers who received spinal analgesia. Tetracaine (Pontocaine) hydrochloride and procaine were the agents used for all patients. Eleven of the mothers of this group received thiopental (Pentothal) sodium to allay anxiety. The largest amount of thiopental sodium given to any mother before delivery was 200 mg.

Group 2 consisted of 165 mothers who received general anesthesia, during the course of which spontaneous respiration was maintained. The agents employed were thiopental sodium, 100 to 150 mg., for induction followed by inhalation of cyclopropane and oxygen. A conscientious effort was made to maintain as light a plane of general anesthesia as was consistent with a quiet operative field. Tubocurarine chloride given in doses of 6 to 9 mg. was an aid in maintaining relaxation, in spite of light planes of anesthesia, and was used for all except three patients in this group.

Group 3 was composed of 157 mothers who received the same agents employed for group 2. The anesthetic technique was modified, however, to allow complete manual control of the mothers' respiration. Relaxant drugs were given three or four minutes following induction with thiopental sodium, 100 to 150 mg., in order to improve operative conditions and to insure complete control of respiration. Tubocurarine chloride was administered to 91 mothers in amounts ranging from 6 to 12 mg., and succinylcholine (Anectine) chloride was given to 66 mothers in total amounts ranging from 40 to 120 mg., given in divided doses. As soon as muscular relaxation was obtained, controlled respiration was begun and continued until the baby was delivered. Respiration was controlled by slowly increasing the pressure on the rebreathing bag during inspiration, followed by sudden release of the bag during expiration. A tidal volume of 500 cc. at a rate of 15 respirations per minute was considered to be adequate. An effort was made, and usually achieved, to acomplish hyperventilation in the mothers with an anesthetic mixture high in concentration of oxygen.

The only essential difference between the two methods of general anesthesia employed was that controlled respiration was used in group 3. The planes of anesthesia were the same in groups 2 and 3, as far as could be determined by clinical signs. The average length of anesthesia before delivery was 15 minutes in group 2 and 12 minutes in group 3.

Evaluation of Newborn Babies

The normal baby flexes its muscles, breathes, and cries immediately after delivery. This is the natural response to birth, and all the babies selected for this study presumably should have responded in this manner. Gasping and whimpering were not accepted as signs of normal response on the part of the baby. On the contrary, they were considered to be signs of distress. The length of time elapsing between delivery and loud crying was used in this study as a measure of the degree of depression of a newborn baby.

Results

Group 1.—Of the 96 babies in group 1, whose mothers received spinal anesthesia, 89 (92.8%) exhibited a normal response to birth during the first minute following delivery. Three infants (3.1%) cried loudly during the second minute after delivery and three (3.1%) during the third minute. Only one newborn infant (1%) in group 1 failed to cry lustily within five minutes after birth.

Group 2.—General anesthesia with spontaneous respiration was administered to the mothers of 165 babies in group 2. Eighty-nine of the babies in this group (54%) responded normally during the first minute following birth. Fifteen babies (9%) cried during the second minute and 20 babies (12%) during the third minute after delivery. A delay in lusty crying of at least three and not more than five minutes was observed in 26 babies (16%), and 15 babies (9%) required vigorous resuscitation for more than five minutes before they responded normally. Therefore, of the 165 babies in group 2, 41, or 25%, were depressed babies by any criteria and required resuscitation for more than three minutes.

Group 3.—General anesthesia with manually controlled respiration was administered to the mothers of 157 babies in group 3. One hundred twenty newborn infants (76.4%) in this group cried loudly within one minute after delivery. Ten babies (6.4%) failed to cry until the second minute after delivery, and 16 babies (10.1%) did not cry until the third minute. Eight babies (5.1%) did not respond normally until three to five minutes after birth. Only three babies (2%) failed to cry lustily within five minutes after being delivered. Serious depression of the newborn infant, as evidenced by a delay in lusty crying of more than three minutes, was present in 11 (7%) of the 157 babies in group 3.

Two relaxant drugs were administered to the mothers in this group. Sixty-six mothers received succinylcholine chloride, and 91 mothers received tubocurarine chloride. The two drugs were not followed by a significantly different incidence of depression lasting less than three minutes (see table). One baby failed to cry within three minutes following the administration of succinylcholine, while 10 babies failed to cry within three minutes following the administration of tubocurarine chloride. The experience with succinylcholine in only 66 patients is too limited to evaluate its usefulness in obstetrics. It would appear, however, to have no greater untoward effect on newborn infants than other muscle relaxants.

Crying Time of Babies Following Delivery After Administration of Tubocurarine Chloride and Succinylcholine

		Minutes					
Relaxant		1st	2nd	3rd	3-5	Over 5	Total
Tubocurarine	No.	67	6	8	8	2	91
	%	73.6	6.6	8.8	8.8	2.2	100
Succinylcholine	No.	53	4	8	0	1	66
	%	80.4	6	12.1	0	1.5	100

Comment

Hypoxia has been shown by Taylor and his associates[4] to occur in newborn babies whose mothers received inhalation anesthesia for their deliveries. It is logical to assume that hypoxia can produce depression of the fetal respiratory center and contribute to the incidence of asphyxia neonatorum. The results of this study support such an assumption.

Control of maternal respiration ameliorated the undesirable effects of general anesthesia upon newborn babies in two ways. Adequate maternal respiration assured an adequate supply of oxygen and removal of carbon dioxide with demonstrated advantages accruing to the infants. The average duration of anesthesia before delivery, when controlled respiration was employed, was 12 minutes, while the average period of anesthesia, when spontaneous respiration was maintained, was 15 minutes. This shorter period of anesthesia may also have been a factor in reducing the respiratory depression in the newborn infants of mothers managed under controlled respiration.

The technique of administering general anesthesia with controlled respiration, which is presented here, was not without its pitfalls. Difficulty in maintaining an adequate airway was the most dangerous of these and was encountered on six occasions. Depression of the newborn infant was noted each time this complication occurred, presumably because of hypoxia and hypercapnia. Endotracheal intubation of the mothers was avoided because it was feared that a period of hypoxia during insertion of the catheter would have a deleterious effect on the babies. In retrospect, intubation seems at times to be the lesser of the two evils and should be employed when it is clearly indicated. On the other hand, most young mothers can be managed easily without endotracheal tubes, and the hazard of intubation can usually be avoided. The danger of inflating the stomach is always present when controlled respiration is maintained without intubation. No harm to patients resulted from this complication. It was found that the pressure on the rebreathing bag could be controlled to keep this complication to a minimum.

Techniques of administration similar in some respects to the method of controlled respiration used in this study have been reported by several authors.[5] Some anesthesiologists prefer to use other agents, some prefer to intubate more frequently, and some reject general anesthesia entirely in obstetrics. There are occasions, however, when general anesthesia is indicated for obstetric procedures. When this occurs, three rules should be observed. The plane of anesthesia should be kept as light as possible. The duration of anesthesia should be as brief as good teamwork by obstetrician, anesthesiologist, and nurses will allow. The mother's respiration should be supplemented by full control of her breathing.

Summary

A group of mothers and newborn infants who were normal by all available criteria and who were delivered by elective or repeat cesarean section were selected for study. Three types of anesthesia (spinal, general anesthesia with spontaneous respiration, and general anesthesia with controlled respiration) were employed. Careful evaluation of depression of the newborn infants was recorded in each instance.

The incidence and severity of depression in the babies was found to be least when spinal anesthesia was given. The babies delivered of mothers who received general anesthesia and had adequate pulmonary ventilation by controlled respiration had a significantly lower incidence and severity of depression than the babies delivered of mothers who received similar anesthesia but who did not have their respirations controlled. It is postulated that better oxygenation combined with better elimination of carbon dioxide for mothers and babies contributed to this result.

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FIVE-YEAR STUDY OF BENZTROPINE (COGENTIN) METHANESULFONATE

OUTCOME IN THREE HUNDRED TWO CASES OF PARALYSIS AGITANS

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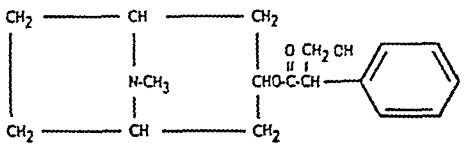
• *Benztropine, a synthetic drug with anticholinergic, antihistaminic, and sedative actions, was administered by mouth to 302 patients with various forms of Parkinsonism. The drug was found to have peripheral curariform effects that are long-lasting, cumulative, and very useful. Doses of 5 to 10 mg. thrice daily caused excessive flaccidity, to the extent that a patient was unable to lift his arm or raise his head off the pillow. Best results, in the control of rigidity, contracture, tremor, and insomnia, were obtained in the dosage range of 1 to 4 mg. a day for older patients and 2 to 8 mg. a day for younger ones. Abnormalities of gait, which troubled 56 patients, were alleviated in 35 of these. Three case histories are given to illustrate the relief from insomnia, night cramps, rigidity, and tremor, the recurrence of symptoms when the drug was temporarily withdrawn, the safety of continued use for more than five years, and the possibility of obviating side-effects, when they do occur, by simultaneous administration of phenindamine and trihexyphenidyl.*

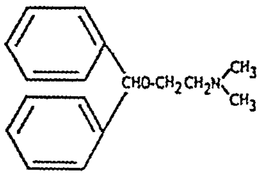
Benztropine (Cogentin) methanesulfonate is a relatively new synthetic drug that has been used for the treatment of Parkinsonism. It has been under study by us at the department of neurology of the College of Physicians and Surgeons and the Neurological Institute of Presbyterian Hospital for more than five years but has been available to the trade only in recent months. A preliminary report of its use by me in 20 patients with paralysis agitans was made in 1952[1] and another report of its effect on tremor in 1953.[2] A considerable amount of literature has since accumulated.[3] However, because of misunderstandings as to posology, actions, and side-effects of the drug and because in a chronic ailment the long-term effects are as important as the immediate outcome, it was considered desirable to record our long experience with use of the compound in over 300 patients.

Chemistry and Pharmacology

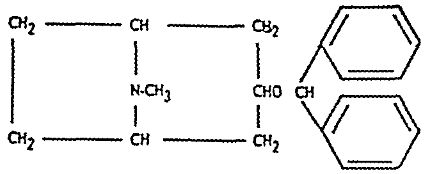
Benztropine is tropine benzohydryl ether methanesulfonate. It was synthesized by uniting the tropine portion of the atropine molecule with the benzohydryl portion of diphenhydramine (Benadryl) hydrochloride to form a new product. Benztropine has the pharmacological properties of a powerful anticholinergic and antihistaminic agent in a single compound. The sedative effect of benztropine in experimental animals is about the same as that of tripelennamine (Pyribenzamine) hydrochloride but much less than that of diphenhydramine. Tests with animals proved it to be an extremely nontoxic compound.[4]



Atropine



Diphenhydramine



Benztropine

Material and Procedure

Benztropine was studied for therapeutic effects, side-effects, dosage, and method of administration in 342 patients. This report is concerned with only 302 patients, because 40 could not be followed up. Of the 302 cases of Parkinsonism, 65 (22%) were postencephalitic, 123 (41%) idiopathic, and 114 (37%) arteriosclerotic. There were 171 (57%) males and 131 (43%) females in the series. Forty-five per cent of the patients with postencephalitic paralysis agitans were in the 40-to-50-year age range, 50% of those with idiopathic disease were in the 50-to-60-year age range, and 67% of those with arteriosclerotic Parkinsonism were in the 60-to-70-year age range. Eighty-one cases were treated at Vanderbilt Clinic and 221 in private practice. The patients were unselected, except insofar as they presented symptoms that were uncontrolled by other remedies.

Benztropine is now available in 2-mg. quarter-scored tablets. Originally, it was administered by us, under the name of MK-02, in amounts of 5 to 10 mg. three times a day, in efforts to establish the limits of therapeutic safety. At such dosages it was found that severely rigid parts turned flaccid to the extent that a patient was unable to lift his arm or raise his head off the pillow. Further trials proved that best results are obtained in the dose range of 1 to 4 mg. a day for older patients and 2 to 8 mg. a day for younger ones. The drug appears to exert a peripheral curariform-like effect that is cumulative and long-lasting; hence, the

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total daily dose may be administered once a day upon retiring. Although a powerful muscle relaxant, it lacks the cerebral stimulant action of other compounds, so that most patients require the administration of an additional drug such as trihexyphenidyl (Artane) hydrochloride, cycrimine (Pagitane) hydrochloride, or dextro amphetamine (Dexedrine) sulfate during the day for maximum benefits. The usual starting dose of benztropine is 1 mg. at bedtime for older patients and 2 mg. for younger ones, and this is progressively increased to the level of optimum effect or maximum tolerance, whichever comes first. Some patients prefer to use benztropine twice a day, with the largest increment at bedtime.

Patients were seen at weekly intervals at commencement of therapy and at longer intervals after the tolerance and response were established. They were under close supervision by telephone during the initial stages of therapy, so that changes in medication could be effected as required. Placebos were administered to some patients for control studies, and others were required to cease taking benztropine for a week at a time so that changes in their conditions could be noted. During visits at office and clinic, observations were made of improvements in behavior, speech, gait, rigidity, tremor, posture, and facial expression. Records were kept of information submitted by the patients and their families. Twenty of the patients were under treatment with benztropine as inpatients of the Neurological Institute, where opportunity was afforded for daily observation of its effects in comparison with effects of placebos and of benztropine in combination with other preparations. A patient's condition was classified as improved or unimproved. In previous studies evaluating the merits of anti-Parkinson agents,[5] it was found undesirable and unsatisfactory to delineate shades of improvement. Patients who gained remarkable relief from benztropine therapy were thus grouped along with those only slightly improved. Moreover, no patient was considered to be improved unless he had received the drug for at least four weeks.

TABLE 1.—*Results of Treatment with Benztropine in 302 Patients with Paralysis Agitans*

		Improved				Unimproved			
		Private		Clinic		Private		Clinic	
Type	Cases, Total No.	No.	%	No.	%	No.	%	No.	%
Postencephalitic	65	12	18.5	2	3.2	27	41.3	24	37.0
Idiopathic	123	75	61.1	18	14.6	10	8.1	20	16.2
Arteriosclerotic	114	14	38.6	6	5.3	53	46.6	11	9.5
Subtotals Private	221								
Subtotals Clinic	81								
Total	302	131	59.2	26	32.1	90	40.8	55	67.9

Results

The results obtained with benztropine in a series of 302 cases of paralysis agitans, with the three types of the disease represented, were evaluated on the basis of the afore-mentioned criteria. A summary of the overall efficiency of the drug is presented in table 1. Here it is noted that the percentage of improvement was greater in the private than in the clinic patients (59% to 32%). In part, this was due to the fact that some clinic patients were seen by different physicians, some of whom were not fully acquainted with the new product and who hence shifted patients to treatment with more familiar compounds such as trihexyphenidyl. In other instances, the medicament, during the long course of a five-year investigation, would be changed from benztropine to other experimental drugs that were under special investigation at the moment. These situations were not likely to occur in private practice, where patients were seen year after year by the same examiner.

TABLE 2.—*Effects of Benztropine on Individual Symptoms of Parkinsonism (302 Cases)*

	No. Reporting Symptom		Improved		Unimproved	
Symptom	No.	%	No.	%	No.	%
Rigidity (contracture)	293	97.0	174	59.5	119	40.5
Tremor	255	82.0	85	33.4	170	66.6
Akinesia	114	37.7	35	30.7	79	69.3
Gait	56	18.6	35	62.5	21	37.5
Spells of "freezing"	53	17.3	37	70.0	16	30.0
Insomnia	51	16.9	29	57.0	22	43.0
Poor posture	38	12.6	16	42.1	22	57.9
Oculogyric disturbances	31	10.3	13	41.9	18	58.1
Sialorrhea	18	6.0	11	61.1	7	38.9

The best results (table 2) were obtained in the control of rigidity, contracture, tremor, gait disturbances, and insomnia. Gait was improved in 62% of the patients. The control of insomnia in 57% is probably attributable to the diphenhydramine component, which has a mild soporific action. Benztropine was found to exert a highly selective action against certain symptoms of Parkinsonism such as no other current drug affords. Chief among these were the fixed facies, dysphonia, dysphagia, faulty posture, muscle cramps, and "freezing" of the legs. Clinical experience in case after case served to prove that benztropine is the most powerful orally given antispasmodic for combating attacks during which the patient's legs become "glued to the ground" and efforts to free himself result in falls and injuries.

Trihexyphenidyl was the most common supplementary drug employed with benztropine (52% of cases). Cycrimine was added in 20% of cases and dextro amphetamine in 10%. Twenty-four patients received benztropine alone throughout the duration of treatment. A combination that proved to be well tolerated and helpful to patients of highly sensitive make-up included 2 mg. of trihexyphenidyl twice a day, one tablet of phenindamine (Thephorin) tartrate three times a day, and 1 or 2 mg. of benztropine on retiring. The fact that benztropine has to be used along with other drugs is no detriment, since it is well known[6] that in order to control the many symptoms of Parkinsonism one not infrequently has to employ several preparations at the same time. What is of prime concern to the patient is that he be made physically more comfortable and functionally more useful at home, at work, and in his social life.

The duration of use of benztropine is shown in table 3. Nine patients have received the drug for over four years. Considering that when the investigation commenced five years ago there were but 20 patients receiving benztropine, the fact that 9 patients (45%) have steadfastly continued receiving the compound reflects very favorably upon its value to them. Again, three years ago only 62 patients were under treatment with benztropine. Of this number, 41 (57%) have maintained its use for upwards of three years, which similarly reflects the long endurance of its good effects. As information accumulated with regard to its efficacy and safety, more and more patients were started on benztropine therapy, many of these during the past year. Under the circumstances, it is of no small significance that, even with the recently added patients, 42.1% of the entire series of 302 patients are listed as having continued with the drug for 18 to 24 months. It should also be noted that private patients continued benztropine therapy almost twice as long as clinic patients, for reasons already stated. It has been our experience that patients derive positive benefits from the new drug and hence continue taking it month in and year out. Even those that discontinue taking it for one reason or another soon find that no other preparation can reproduce its singular effects and thus resume treatment with it. There is little, if any, increase in tolerance, so that most patients do not require an increase in dosage with the passage of time. Since benztropine is administered but once a day, at bedtime, its administration is easily added to any medicinal program.

TABLE 3.—*Duration of Use of Benztropine Among 302 Patients with Paralysis Agitans*

	Months																	
	Less than 6		6-12		12-18		18-24		24-30		30-36		36-42		42-48		More Than 48	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
221 private patients	44	19.1	177	80.9	137	62.0	112	50.6	87	39.4	60	27.1	39	17.7	22	10.0	9	4.8
81 clinic patients	47	58.0	34	42.0	26	32.2	15	18.5	10	12.4	8	9.9	2	2.7				
Total (302 patients)	91	30.2	211	69.8	163	54.0	127	42.1	97	32.1	68	22.5	41	13.6	22	7.3	9	3.0

Side-Reactions

No serious side-reactions appeared in any of the 302 patients. The chief side-effect has been dryness of the mouth (53.3% of patients). This is usually mild in nature and disappears after breakfast. In only 5.3% of of the patients was the dryness sufficient to require an adjustment in dosage. A macular skin rash appeared on the arms and legs of a few patients (1%). This cleared on temporary withdrawal of the drug or reduction of the dose. Weakness occurred with great frequency during the early stages of the investigation. However, it became apparent that this was due to the extraordinarily large doses that were being used, and after the dosage was reduced this symptom was not noted. Drowsiness, dizziness, or mental confusion were not encountered in the 221 privately treated patients. However, six such instances were recorded by different observers in the 81 patients treated at Vanderbilt Clinic. Slight nausea was present in 3.7% of the patients and blurring of vision in 3%. Benztropine showed no deleterious effect on the blood of 130 patients in whom serial studies were made. It can be said that benztropine is one of the safest drugs to use, because it causes minor, if any, blurring of vision, does not affect the blood, blood pressure, pulse, or heart, and does not produce drowsiness, dizziness, mental fogginess, or hallucinations such as not infrequently occur with other anti-Parkinson agents.[7] Benztropine is safe to employ in patients with glaucoma, because within therapeutic range the pupils are little, if at all, affected.

Report of Cases

The following cases will illustrate practical situations met with in the administration of benztropine and some of its effects and side-effects.

CASE 1.—A 56-year-old patient with idiopathic paralysis agitans had a six-year history of progressive bilateral tremor and rigidity, stooped posture, propulsive gait, frequent falls, insomnia, and mental depression. He had been treated with a variety of drugs, the last of them being trihexyphenidyl. He was particularly distressed by his inability to turn in bed or to get in and out of bed. His wife had to rise several times a night to get him safely to the bathroom. In April, 1951, he started taking 2 mg. of benztropine on retiring in addition to trihexyphenidyl during the day. A month later, the patient was able to walk with greater ease, his posture had improved, and he was happy to report that he was able to get in and out of bed by himself. His wife was especially pleased, because for the first time in years she was able to enjoy a full night's rest. He continued to maintain his improvement until recently, when some progression in rigidity made it necessary for him to take 1 mg. of benztropine at noon. There have been no side-reactions.

CASE 2.—A 64-year-old x-ray technician had idiopathic paralysis agitans of five years' standing, manifested chiefly in tremor and rigidity of the right side of the body. After unsatisfactory trials with other remedies, he started receiving 2 mg. of benztropine at bedtime in October, 1952, and reported remarkable control of his symptoms. His wife stated that with the new drug "her husband does his work regularly, is cheerful, active, visits friends, and converses easily, whereas previously his speech was thick, his limbs ached and cramped, and the tremor proved embarrassing to him." He made no complaint of side-reactions during any of his visits. However, in May, 1954, in the course of a routine blood check, it was discovered that he had chronic leukemia, with a white blood cell count of 86,000. Benztropine was immediately suspected by the patient, but further investigation proved that our patient's failure to employ necessary precautions in his x-ray work was to blame. With institution of rigid precautions, his white blood cell count returned to normal. He has continued to do well while receiving 2 mg. of the drug and has not needed to increase the dose or to add other preparations.

While in most cases benztropine had to be supplemented with other drugs, there were instances, such as in case 2, where patients employed benztropine alone with good effect. This case also serves to point up the lasting action of the dose given at night and the protection it affords the patients against tremor and rigidity throughout the succeeding day. The case further illustrates a ready tendency of patients to attribute all physical discomforts and disturbances, in this instance leukemia, to a new drug. Complaints patients require discriminating evaluation.

CASE 3.—A 58-year-old man had arteriosclerotic Par with typical onset of shuffling gait and rigidity o extremities in 1952. There was an antecedent hi en. Again we must in all fairness doff our hats to the practitioner whose vast knowledge of care of persons from infancy to old age is being greatly enhanced. Then, too, the various disciplines (specialties) of medicine have played a very impressive part in this vast kaleidoscope of medical care. It has not been too long ago that a fractured femur in an older person was a warrant either for his demise or, at best, for life in a chair or bed. Especially unpleasant were the experiences of the hemiplegic patient with aphasia who was considered mentally deteriorated; or the arthritic, a useless mass of vegetating humanity; or the amputee consigned to a chair for life, to be lifted from place to place. Often they had been handed from hospital to hospital, service to service, and from physician to physician until the lowest depths of physical degradation had been reached.

There remained but one course to follow, transfer to a public institution where lack of home comforts and curtailed (and even severed) contact with family and friends made for difficult adjustment. A tax-supported facility, the Woodville and Mayview hospitals of the Allegheny County Institution District, enlisting the aid of its staff, consultants, and community resources, has performed a magnificent feat of restoring many of the above-described "displaced persons" to home and community. These accomplishments, in brief, consisted of combining the expertness of all medical specialties where needed with the ancillary services so necessary in the program. Early ambulation for patients with fractures, graded activities for the hemiplegic, utilization of the remaining abilities of the arthritic, and training of the amputee to be self-sufficient were integral parts of the process. Here again is represented the factual status of rehabilitation for an aging population that will grow larger.

We also see the collective efforts of the medical profession, frequently criticized, infrequently praised, directed toward the ill and aging. This road has not been a smooth one. Progress is often obstacle ridden—which only makes for greater effort. There are many gaps in our efforts that will close as greater understanding gives us enlightenment. First, housing for the recovered older person is scarce and abominable. Discharge from a public institution is a ticket to a fourth or fifth-floor walk-up, cold flat; this "ascension" to higher levels is purely a monetary method of saving finances—the more stairs climbed, the cheaper the rent. It would appear that all housing projects should provide proper cover for these humans at a compatible rental. Second, far too often formerly disabled aging persons languish in "home departments" of public institutions. Many of these people are able to be up and about but have unfortunately acquired the institutional stamp as an easier way of life. There are, however, certain statutes that prevent their discharge, since suitable housing is unavailable and the desire to live independently has been lost.

Third, many public assistance bureaus act as fiscal agents, doling out finances to needy clients, whereas their prime function should be the maintenance of the older person in familiar surroundings outside a public institution. Fourth, occupational opportunities must be appraised by labor, industry, and community to lighten the financial burden, as well as enhance the dignity and self-sufficiency of these persons. Finally, the public must be educated to the understanding that age, even with disability, is not necessarily the last station before demise. This, by all odds, is the most difficult obstacle to surmount, but the concerted drive by medicine and its companions and the social, economic worlds of communication will eventually dispel the hopelessness, helplessness, and haplessness of our aging population.

In the immediate future a new institution for the chronically ill and aging will be completed. It is being built under the auspices of the government of Allegheny County (near Pittsburgh) and will embody the most modern concepts of medical care and architecture. Of course, obsolescence comes rapidly in this field. However, there will be adequate and complete medical facilities, opportunities for most of the facets of rehabilitation, recreational advances, and, above all, a structure built specifically for its planned purpose. This might be criticized by the smaller and less opulent communities, but it will be a model and may be adjusted to the needs of any locality. The team approach, the basis for the success of its original venture of physical rehabilitation of the chronically ill and aging, will be maintained and increased in scope.

Comment

The foregoing report sketchily represents 10 years' experience in the care of the aging and chronically ill, including visits to 200 or more institutions in this country and abroad. It is intended to point out the possibilities for physical redemption and morale resumption in a group who sorely need help. In the total consideration, those in physical medicine deserve commendation for their part. This mass effort belongs to no single group, since each is interdependent upon the other. Evidence favoring the physiatrist and his staff can be found not only in public and private hospitals but in Veterans Administration institutions, where separate services have been inaugurated to facilitate and make workable the expertness of all other specialties. The poorhouse ("gateway to oblivion") must give way to a more modern hostel where adequate and more all-embracing medical care must be available for better restorative services.

The specialists of medicine are working increasingly, delving into the mysteries of the aging process and prevention of physical catastrophies as well as the means of offsetting their undesirable sequelae. Those in physical medicine in particular are charged with the responsibility for putting into conjunctive action the expertness of their colleagues in all other specialties. Finally, this is a medical problem and, like all others preceding it, has challenged the tenacity and ingenuity of all who are directly or indirectly involved. This challenge will be met!

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SURGICAL TREATMENT OF HIGH-LYING GASTRIC ULCER

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• *Two varieties of surgical operation are applied to high-lying gastric ulcers. One consists in resecting the ulcer (if it is on the lesser curvature) with all or part of the lesser curvature and a sufficient part of the greater curvature to give a two-thirds resection; this is followed by repair according to either the type 1 or type 2 Billroth operation. The other consists in leaving the ulcer undisturbed, resecting the distal one-half or two-thirds of the stomach, and concluding according to either the Hofmeister or the type 1 Billroth operation; the ulcer heals without trouble in most instances. Both varieties of operation have given excellent long-term results. In either case, specimens of tissue must be obtained and examined for malignancy, which is the greatest problem in the treatment of high-lying gastric ulcers. The unexpected finding of malignancy by microscopic examination is most common in small ulcers. Concomitant gastric and duodenal ulcers are frequent, and among 98 cases of this kind there was marked retention. When obstruction occurs it must be relieved. The temporary insertion of a gastrotomy tube for feeding is to be considered if obstruction is severe, and a posterior gastroenterostomy may be advisable in poor-risk patients.*

The surgical problem in duodenal ulcer is a fairly standard one, and the diagnosis is usually clear-cut, except in an uncommon case where the source of hemorrhage is unknown. The types of operative procedures are standardized, with each one having numerous advocates who can quote a large collected series to show the results that can be achieved. The surgical problem in gastric ulcer, however, is not so well standardized; and there is a less clear-cut picture as to the most desirable treatment, particularly for the 5.5% of gastric ulcers that are found in the cardia.[1] The greatest problem is one of diagnosis; the question as to the differentiation between gastric ulcer and carcinoma is not completely solved except by microscopic section.

Incidence of Malignancy and Hemorrhage

Gastroscopic examination of 273 patients by Schindler and Desneux[2] resulted in a 7.3% diagnostic error. Eighteen benign lesions were diagnosed as cancer, and two cancers were diagnosed as benign lesions. In 14, the lesion could not be examined adequately. Ranson[3] reported that the surgeon found an unsuspected carcinoma in 10% of 188 gastic resections for benign ulcer. Caruolo, Hallenbeck, and Dockerty[4] reported 91 posterior wall peptic-type ulcers, which required sharp dissection to detach the ulcer base from adherent structures. Three of the 91 proved to be carcinoma. Twenty-six of 88 patients, or 29.5%, were thought to have carcinoma in view of x-ray findings. The final preoperative diagnosis was carcinoma in 36, or 40.9%, of the patients. But every one of these patients proved to have only a benign lesion, though three patients had total gastrectomy. Three others who did have carcinoma had free acid; the lesions of all these three had been diagnosed by x-ray as benign. Ivy,[5] in a special study on the presence of malignancy in gastric ulcers diagnosed as benign, found that 281 of 2,212 cases were carcinoma, an incidence of 12.7%. These examples simply emphasize the fact that not even the most experienced doctor can adequately differentiate between benign and malignant gastric ulcer on the basis of the patient's age, the clinical picture, the presence or absence of free acid, the gastroscopic or x-ray examinations, or surgical palpation and excision.

Numerous reports have emphasized the frequency of concomitant gastric and duodenal ulcers in patients requiring surgical intervention for peptic ulcers. Johnson[6] quotes Sir David Wilkie, who reported 42 of 300 personal cases in which combined ulcers occurred, an incidence of 14%. In Johnson's own series there were 29 of 311 cases, or 9%, of combined ulcers; Ranson[3] reported a 16.5% incidence of combined ulcers. In a series of 156 cases, I found combined ulcers in 12% of the patients. Johnson[6] found that the duodenal ulcer was discovered first in 79 of 98 cases, while the gastric ulcer was discovered first in only 6 cases, in 5 of which there was an old healed duodenal ulcer scar. There was usually hyperacidity, characteristic of a duodenal ulcer, in the combined cases. In 76 of 98 cases there was marked retention. I have had a similar experience, which has impressed me with the fact that duodenal obstruction increases the possibility of later development of gastric ulcer.

Free perforation of high-lying gastric ulcers does not seem to be common, though Meyer[7] reported that 49.5% of 700 perforated ulcers were in the stomach. Hayes[8] reported that only 2% of gastric ulcers with perforation as the presenting symptom were malignant, whereas 16% of all other gastric ulcers were malignant. While free perforation is not common, perforation into other viscera is not uncommon, the pancreas and liver being most commonly involved.

Many authors agree that hemorrhage from gastric ulcers is common. Johnson[6] reported that there was bleeding in 47% of those patients with combined gastric and duodenal ulcers. Taylor[9] found that five of eight acute gastric ulcers of the high lesser curvature hemorrhaged. Branwood[10] found that 84 of 116 bleeding gastric ulcers seen at the Royal Infirmary between 1944 and 1951 were benign and that in about one-half of the cases in which hemorrhage occurred and resection was not done there was a recurrence of hemorrhage. In Ranson's[3] series, 4.8% of the gastric resections were performed for hemorrhage.
Presbyterian Hospital of Chicago,[11] three
had subtotal gastric resections for
fatal postoperative hemorrhage fr
o 7 cm. distal to the esophago

Read before the Section on Surgery, General and Abdominal, at Annual Meeting of the American Medical Association, Chicago, 1956.

Indications for Surgery

Perforation of gastric ulcers into the free peritoneal cavity is an indication for surgery, just as it is in duodenal ulcers. Severe hemorrhage may be an indication for urgent surgery. In the presence of severe bleeding of the upper gastrointestinal tract, where there are none of the signs of portal obstruction, I believe surgical intervention is indicated if the hemorrhage persists after 2,500 cc. of blood replacement. The operation is primarily to stop hemorrhage, though it should heal the ulcer also. The stomach must be opened widely and a search made for the bleeding point. Often this cannot be found, and a three-fourths resection is performed. If severe hemorrhage recurs in the postoperative period, reexploration should be carried out and all the stomach except a 1 cm. margin at the esophagus should be resected. I now know of four instances where this has been lifesaving.

The large adherent gastric ulcers pose a special problem. These usually have perforated so that the liver or pancreas makes up the base of the ulcer. The usual diagnostic aids are not reliable. However, a two-to-three-week course of intensive medical management, often using a milk drip at night, will promote healing. If healing is not complete within this time, surgery is indicated. Many of these patients are in the older age group and their acid values are low. Sometimes no free acid can be found by an Ewald test meal. Pain is not prominent in these large ulcers. A rapidly enlarging ulcer likely will be found, on x-ray examination, to be benign [12]; the large adherent ulcers are more apt to be benign than malignant. At the time of operation, the stomach should be opened and numerous biopsy specimens taken to determine the nature of the lesion, whenever there is doubt as to the diagnosis. In all cases in which gastric ulcers have not healed after three weeks of medical management resection should be done.

A review shows that in 75% or more of gastric carcinomas masquerading as benign lesions resection is possible and that 35% to 40% of those patients with such lesions survive five years after their operation. Thus, 30% of all patients with malignant ulcers with a preoperative diagnosis of benignancy are alive five years after operation.[13]

Types of Operative Procedures

There are two common operative procedures that are applicable to high-lying gastric ulcers. One of these, the operation of choice as reported by Johnson and Orr,[14] is the resection of the ulcer with all or part of the lesser curvature (if it is a lesser curvature ulcer) along with a sufficient part of the greater curvature to give a two-thirds resection. A Billroth 1 or 2 repair is then performed. Shoulders and Lischer [15] advised that the large ulcers be treated by a subtotal gastric resection. They recommend that the rim of the ulcer be resected but that the base should not be disturbed. Caruolo and co-workers [4] say that the surgeon faced with a case of large, fixed ulcerating lesion of the posterior wall of the stomach without signs of malignancy should remember that most lesions of this type are benign and they should, therefore, proceed with resection, whenever possible, thus avoiding the error of regarding the lesions as malignant and inoperable. None of their 91 patients with adherent ulcers of the posterior wall developed pancreatitis when the ulcer base was dissected off the pancreas. Waltman Walters [16] has said he prefers this type of operation. I have performed this type with complete satisfaction. Maingot [17] uses the Pauchet type of resection, which is only a little different, except that he cauterizes the remaining base of the ulcer if it cannot be removed.

The second most common type of operation, which was described by Madlener [18] in 1923, is popular in Europe. In this operation the high-lying adherent ulcer is not disturbed. The distal one-half or two-thirds of the stomach is resected, and a Hofmeister or Billroth 1 type of resection is performed. The ulcer site heals without trouble in most instances. Colp and Druckerman [19] strongly recommend this operation in poor-risk patients. With this operation Finsterer [20] reports an operative mortality of 5%.

With either type of gastric resection the long-term results have been excellent. Unsatisfactory results or occurrence of jejunal ulcer is uncommon after resection for gastric ulcer. For all types of gastric ulcer Ranson [3] reported only 5% poor results and 3% occurrence of jejunal ulcers. Other authors are in general agreement with him. Total gastrectomy may be performed, but it often disables the patient and should not be done if malignancy can be ruled out. If the patient is in poor condition, a simple gastroenterostomy may be an immediate way out. I have seen a patient with an immense, high-lying gastric ulcer that had the capsule of the liver as its base who recovered after gastroenterostomy and remained well for many years. A temporary gastrostomy tube may be placed in the normal part of the stomach to facilitate feeding when there is obstruction in the upper one-third of the stomach. Since wedge resection of the ulcer does not reduce the acidity or relieve obstruction, it is inadequate.

Summary

The greatest problem in the surgical treatment of high-lying gastric ulcer is the question of malignancy. Either the ulcer must be resected and examined microscopically or numerous frozen-section biopsy specimens must be examined to rule out malignancy. The large adherent ulcers are usually benign, and the unexpected finding of malignancy by microscopic examination is most common in small ulcers. In cases of severe hemorrhage the ulcer must be resected and the acidity reduced. Concomitant gastric and duodenal ulcers are common, and obstruction must be relieved in all cases. A two-thirds resection with resection of the gastric ulcer, which is the treatment of choice, will usually give good results. The Madlener operation, leaving the high-lying ulcer and performing a two-thirds resection of the distal portion of the stomach, has given good results for many. In poor-risk patients, it may be wise simply to perform a posterior gastroenterostomy, and, if there is a severe obstruction, to insert a temporary gastrostomy tube in the stomach for feeding purposes.

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THERAPEUTIC EXERCISES IN MANAGEMENT OF PARALYSIS AGITANS

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• *The prevention of progressive disability in a patient with paralysis agitans is dependent to a great extent on the patient's ability and desire to be active. The muscular rigidity, discouragement, and even depression so characteristic of this illness are not conducive to activity. The recent emphasis on medical and surgical therapy, which often are themselves palliative, has obscured the importance and often prevented the use of continuing exercise in the treatment of this disease.*

Specific exercises prescribed by the physician to prevent contractures and to increase speed of the extremities, along with correction of posture and training in gait, contribute much to the treatment of this disease. In addition, it is necessary to urge the patient to continue to perform the activities of daily living, as well as other tasks requiring use of his muscles, to prevent the deleterious effects of inactivity.

Paralysis agitans is a progressive symptom complex of adult life for which there is no curative therapy. Parkinson described it as[1]: "Involuntary tremulous motion, with lessened muscular power, in parts not in action and even when supported; with a propensity to bend the trunk forwards, and to pass from a walking to a running pace: the senses and intellect being uninjured." This syndrome is characterized by the frozen expression of the face, the festinating gait, "pill-rolling" tremor, stooped posture, and increased rigidity of the muscles of the extremities and neck. The last symptom, along with the other debilities, causes a diminution of the speed and range of movement and progressively handicaps the patient. As a consequence, he frequently withdraws from activity and social contacts and becomes increasingly dependent, depressed, and disabled.

The prevention of progressive disability in many patients who have paralysis agitans depends to a great extent on their ability and desire to be active. The muscular rigidity, discouragement, and even depression so characteristic of this illness are not conducive to such activity. Recent emphasis on medical and surgical therapies, which, in themselves, may be only palliative, has obscured the importance and often prevented the use of continuing exercises in the treatment of this disease.

While not of help in preventing the tremor, specific exercises prescribed by the physician to prevent contractures and to increase speed of motion in the extremities, along with correction of posture and training in gait, are important in the management of paralysis agitans. In addition, it is necessary to urge the patient to continue to perform the activities of daily living as well as other tasks requiring use of his muscles to prevent the deleterious effects of immobility.

Therapeutic Exercise

Patients should be instructed by physician or physical therapist under the physician's supervision in a program of simple exercises to be performed at least three times daily. Instruction is given first in exercises to obtain and maintain normal range of motion of all the joints in the extremities in order to prevent contractures. For example, to exercise the shoulder, the patient raises the arm forward and upward over the head and then sideways upward over the head. Also, the patient places the palm of the hand on the back of the neck, then rotates the shoulder and extremity until the back of the hand is placed on the shoulder blade. These movements maintain full range of motion in the shoulder.

For the elbow, the forearm is flexed until the finger tips touch the shoulder, and then the elbow is fully straightened. The remaining joints of the upper extremity, especially fingers, are flexed and extended to the fullest extent. The exercises for the fingers are supplemented by occupational therapy, such as craft

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From the Mayo Clinic (Drs. Erickson, Clark, Mulder, and MacCarty) and the Mayo Foundation (Drs. Erickson, Clark, Mulder, MacCarty, and Clements). The Mayo Foundation is a part of the Graduate School of the University of Minnesota.

Read before the Section on General Practice at the 105th Annual Meeting of the American Medical Association, Chicago, June 13, 1956.

work, which is valuable for coordination and speed of movement of fingers. The lower extremities are exercised in a similar manner with stress on full range of motion of each joint. It is important for patients to obtain full extension of the hip, and, also, the patient should be instructed to extend the back, when lying prone, by lifting head and shoulders from the position of rest. This exercise strengthens the extensor muscles of the back and neck. These movements are repeated 5 to 10 times, three times a day. The patients are encouraged to practice the movements with increasing speed to aid in reducing the rigidity. Some patients have noted that these simple exercises are helpful in reducing rigidity temporarily, so that some difficult task, such as writing, may be performed more easily.[2]

The relationship of the neck is important in the maintenance of good posture. Limited motion of the neck is common in these patients and has an adverse effect on posture and gait.[3] Active movements of the neck in all directions, especially rotation and extension, are encouraged to maintain range of motion. The patient is trained also to correct his posture by practicing standing as tall as possible with head up, chin in, and chest up. The lower part of the abdomen is held in and up, and the hips are rolled under the body to reduce lumbar curve. To facilitate the correction of posture, the patient is taught to stand with heels, hips, shoulder, and head against a wall. The lower part of the back should be pressed toward the wall to reduce the lumbar curve. The patient should attempt to hold this posture whenever standing or walking. Although most of the patients are in older age groups and senile posture changes are common, every effort is made to have them correct the posture at all times.

Special attention is paid to the gait, because most of the patients have the usual difficulties such as propulsion and a shuffling of their feet, which are intensified by poor posture. They are encouraged to walk with a heel-toe gait, bending their knees so that the shuffle is eliminated. The training should include practice in climbing stairs and also making turns. The lack of associated movements of the upper extremities is obvious, and the patient is urged to swing the arms in the normal manner when walking, although it is often not possible.

In addition to the rigidity and difficulty in initiating active movements, the extensor muscles in the lower extremities may be weak. For example, in addition to trouble in initiating movement, frequently the quadriceps muscles are weak and the patient will have difficulty in getting in and out of chairs or climbing stairs. The power of the muscles can be increased by a program of progressive resistance exercises.[4] The patients are instructed to do these exercises once a day, using sandbags that are hung over the foot for weight. It is important that the amount of weight lifted by extension of the knee be increased progressively, usually every week. The number of contractions is limited to 30 in three series of 10 contractions each, first lifting one-half, then three-fourths, and finally the full or maximal weight in one series of 10 contractions. This same program of strengthening exercises may be used for other groups of weak muscles.

Occasionally the patient with paralysis agitans may have considerable limitation of motion of the shoulders or other joints as a result of lack of use and rigidity. It may be necessary to prescribe heat from a simple lamp followed by sedative massage, and the simple exercises as outlined will have to be more strenuous in order to improve the range of motion of the joint. For the shoulders the active exercises may be supplemented by having the patient use an overhead pulley, with each hand holding an end of the rope. In this manner, one arm assists the other to obtain more abduction. An explanation of the purpose of these exercises is an important part of the instruction, so that the patients will be motivated to continue them indefinitely.

Activities of Daily Living

We believe that the continued performances of the usual common tasks of daily living are of paramount importance in the treatment of patients with paralysis agitans. The frequently progressive inability to perform the usual activities and the tendency of friends and family to take over lead to increasing depression and apathy, which may become so severe as to require psychiatric therapy. As the disease progresses, lack of mobility results in contractures that may render the patient bedfast and the outlook hopeless.

In order to arrest this relentless downhill course to immobility and to help ameliorate the symptoms of rigidity, it is necessary to convince the patient and his relatives that he must return to as many activities of daily living as possible. Those common tasks, which may improve the rigidity or prevent its rapid progression, include such everyday occupations as dressing oneself, gardening, and walking. Improvement of mental attitude may be encouraged by sports, such as golf and games, which aid the patient in socializing and help him avoid excessive rumination about his illness. Of paramount importance are those gainful activities such as maintenance of the home and business, which give the patient a sense of achievement. Even though these activities are poorly performed, the patient must be urged to continue them. His family must be willing to encourage him and allow him to complete these tasks unaided. Emphasis must be placed on the fact that the treatment of this disease is concerned with a constant struggle to keep active and thus is a "full-time" job for the patient. In addition, the patient must understand that his goal must be palliation or the prevention of further progression of the disorder rather than cure. While these activities as well as medical and surgical therapy are not curative, the energetic use of all these modes of therapy, when indicated, will usually retard or halt the progressive disability. In some cases there may even be encouraging improvement.

Concerning these patients Parker[5] stated: "Emphasis should be placed on their retention of intellect and the need of carrying on as they have been doing and for as long as they can. They should go on with their flags flying and their guns firing in a useful existence as long as they are able. Resignation is a fatal step for them."

Summary

The prevention of the progressive disability in many patients with paralysis agitans depends to a great extent on their ability and desire to be active. In addition to specific exercises prescribed by the physician, the patient should be encouraged to continue the activities of daily living in order to prevent the deleterious effects of immobility. While both the medical and surgical treatment of these patients are of importance, their use should not be allowed to obscure the value of continuing exercises in the treatment of this disease.

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PHILOSOPHY OF RETIREMENT

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• *Retirement from one's life occupation is inevitable, and the problem of making it spiritually, physically, and financially comfortable is more important than ever. Seven questions here stated must be answered, especially questions of location and income. If an individual finds the solution that fits his own situation, it becomes easy to develop former interests into avocations that are absorbing, congenial, constructive, and peaceful.*

The problem of when, where, and how to retire from one's work and occupation has to be faced by everyone if he lives long enough. With increased longevity and life expectancy of the population of the United States nearing the age of 70 years, more people are retiring from their life occupations than ever before. Many more professional and business organizations are retiring their personnel at age 65. The wear and tear of the surgeon's life, in many instances, makes retirement mandatory at 65, if not earlier. So the problem of retiring and how to do it is more important than ever.

The first few weeks of retirement may seem like a much-needed vacation, and, if spent in the congenial surroundings of air, water, and sunshine, they may be a delightful experience. But, after a few weeks of loafing and expensive resort bills, and with no occupation, life begins to pall and the idea of returning home, with no promise of former duties or new avocations, becomes more and more of a nightmare.

For these reasons it becomes imperative to plan and prepare for the sunset of life, if it is to be relatively comfortable spiritually, physically, and financially, as well as pleasant and worthwhile to yourself and your family. Avoid above all else the tragedy of becoming an unoccupied, degenerating vegetable. This has happened to many luckless souls who had not anticipated and planned for retirement, and this may happen to anyone who has no avocation or a sense of humor or the joy of living.

Inasmuch as senescence begins at birth and imperceptible gradations of aging continue through the years, everyone has time to prepare for retirement. We grow older every day, and the only way to avoid old age is to die young, but this has nothing to do with the subject at hand.

Hobbies

Because an interesting occupation, an avocation, is essential to the happiness and success of retirement, it must be discussed first. Borodin, the famous Russian musician and composer, was primarily a physician and professor of chemistry. His hobby was music, and he defined it as "a recreation, a pastime, an avocation, that distracts me from my principal activity as a professor." Avocations or hobbies are of all sorts and kinds. They vary from the sublime to the ridiculous. As long as they serve their purpose of giving one congenial occupation it matters not what they are. Studying the theory of relativity may be at one end of the hobby spectrum, collecting epitaphs from moldy tombstones at the other. A sense of humor is of tremendous advantage, but a man without it can still follow a hobby, though it will probably be uninteresting to others. I once knew a serious philologist and clergyman, utterly without humor. His hobby was proving the doctrine of the Trinity. On one occasion at dinner, with watermelon as the dessert, I saw him carve it so that the seeds appeared in groups of three.

Of course some hobbies are far more agreeable to the family and the neighbors than others. Landscape painting, stamp collecting, cooking, and gardening are less noisy than practicing the bull fiddle or the trombone. One thing is certain. It takes time to develop a worthwhile avocation that can be followed and enjoyed after retiring. One should practice and develop it while he is active in his profession or occupation, so that he can enjoy and appreciate it later. This will make him look forward to retirement instead of dreading it, with the knowledge that he will have more time to follow his hobby, or hobbies, for one should have more than one but not too many. Before retiring one has his weekends, and they comprise almost a third of the year. They can be used, misused, or abused, but they do provide time for developing a hobby, without interfering with such other avocations as golf or poker.

There are hobbies that become more interesting and instructive the longer they are followed. One man I know is a wholesale manufacturer of an essential product. He became interested in Persian rugs and carpets. Because of his lucrative business he was able to collect rare and beautiful specimens and now has one of the finest private collections of Oriental carpets in the world. This collecting took him to the Near and Middle East many times and got him interested

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Read before the Section on Surgery, General and Abdominal, at the 105th Annual Meeting of the American Medical Association, Chicago, June 12, 1956.

in the geography, history, and cultures of those countries, as well as in the materials and dyes used in the making of the finest rugs. He is now a leading authority in the periods, patterns, and origins of Iranian carpets and gives lectures in the leading museums of the country. He has a great library on the geography, history, and traditions of Persia, ancient and modern. He is indeed well equipped for retirement.

Another man, a well-known physician in the South, had a heart attack at the age of 60. His doctors made his retirement mandatory. He had been interested in ornithology, so he decided to turn his estate into a bird sanctuary and devote his time to the further study of birds and their habits. In a few months he had made the many varieties of birds that populated the sanctuary so accustomed to him that they would feed on the brim of his 10-gallon hat. He had a marvelous lot of interesting stories about his birds and their ways. A lady whom I know is widely traveled. She has an amazing collection of keys of all sizes, shapes, sorts, and materials which she has found in the different countries she has visited. An Arab physician whom I met in Jerusalem has what is said to be the world's largest collection of amulets. He told me that the blue used in making amulets is the universal color among superstitious and illiterate peoples. Blue is supposed to prevent bad luck and fend off the evil eye. Cultural hobbies as a rule do not require physical exercise, so that in addition to one such hobby it is wise to have another that takes one outdoors, such as gardening, golf, or fishing.

Collecting, like chess, is a universal avocation. Too often, however, it is limited to one or two people. This is certainly true of that wonderful game of chess. It is absorbing to the two that play it, but it is not exciting to the rest of he family. So absorbing it is with its endless positions and combinations that for long periods there is no conversation but only concentration, to make sure that one does not make a move that will give the opponent the advantage that will give him the win and you the loss of the game. Certainly there is no other game in which there is no luck, only the make or break of the play entirely up to the two opponents. Chess is a delightful hobby for two congenial souls, but it should not be taken too seriously, as insomnia and worse may follow.

Preparing for Retirement

In preparing for retirement there are a number of questions that have to be answered if it is to be a comfortable and happy one: 1. Do you know where you would like to retire, and have you made any plans for it? 2. Do you know the amount of money you will need for yourself and your family? 3. Have you saved and set aside any funds for this purpose? 4. Have you insurance annuities, matured policies, or negotiable securities? 5. Have you settled your debts? 6. Are you willing to make a budget based upon your future income, and are you willing to follow it? 7. Is your retirement income too large? Your income will probably be considerably smaller than when you were working. Having a large income when you have retired has some definite disadvantages. It means continued responsibility, too many houses, and too much traveling. Thoreau once said "A man is rich in proportion to what he is able to do without." Lincoln said "wealth is simply a superfluity of what we don't need."

These questions are not pleasant, but they must be answered if you are to have peace and tranquility later. So prepare these answers before you have to retire.

Retirement Compensations for Surgeon

Let me now discuss the compensations for the surgeon when he retires. Time is his own, to do with it as he pleases—a rare experience after the busy life and trying years of his practice. No more anxious hours before, during, and after critical operations and difficult times with the distraught members of the patient's family and his solicitous friends, as well as the friends that consider themselves influential. No more dull and interminable committee meetings. There will be time to follow pet hobbies, to read many books on many subjects that he has not had time for in the busy years gone by, time to resume investigative problems previously attempted or contemplated, time to sit quietly and review leisurely the happy incidents and experiences of his surgical career, and time to contemplate with tranquility, and with faith, the sunset and twilight of life.

John Buchan once said, "As we age the mystery of time more and more dominates the mind. Time goes on, and for us mortals, in only one direction." However, this time motion has been disputed. Henry Austin Dobson said, "Time goes, you say? Ah no! Alas, Time stays, we go." Today the superscientists review the cosmos as a time-space continuum and time and space as a constant. To the relativity of time, motion, and space Einstein contributed more than anyone else, but this idea is better understood by the following verse:

There was a young lady so bright
She travelled much faster than light
She went out one day in a relative way
And returned on the previous night.

Speaking of time and occupation, Longfellow years ago had this to say:

Ah, nothing is too late
Till the tired heart shall cease to palpitate
Cato learned Greek at eighty, Sophocles
Wrote his grand Oedipus, and Simonides
Bore off the prise for verse from his compeers
When each had numbered more than four score years, . . .
Chaucer, at Woodstock with the nightingales,
At sixty wrote the Canterbury Tales;
Goethe at Weimar, toiling to the last,
Completed Faust when eighty years were past. . . .
For age is opportunity no less
Than youth itself, though in another dress,
And as the evening twilight fades away
The sky is filled with stars, invisible by day.

Goldsmith said "O blest retirement, friend to life's decline." James Barrie said, "God gave us memory, that we might have Roses in December." Finally Robert Browning, in his "Rabbi Ben Ezra," said: "Grow old along with me! The best is yet to be, The last of life, for which the first was made."

30 N. Stanworth Dr.

EFFECTS OF SULFONYLUREA DRUGS IN HOSPITALIZED DIABETIC PATIENTS

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• *The antidiabetic effects of carbutamide and tolbutamide were studied in 11 normal and 7 diabetic subjects. Doses of 2 gm. of either drug given by mouth under certain standard conditions produced a lowering of the blood sugar level in 10 of the normal subjects. Case histories of the diabetic subjects here given show that only one had a prompt and completely satisfactory response; another had a delayed but ultimately satisfactory response. The responses of the remaining patients were unsatisfactory, and in two the drugs were entirely ineffective. Mild, transient leukopenia was observed twice. Since five of the diabetic subjects had been selected as suitable candidates for sulfonylurea therapy on the basis of previous reports, it appears that the indications and limitations of these drugs require further study.*

Apparently the first report of depression of the blood sugar level by a drug of the sulfonamide group was made in 1942 by Janbon and his associates,[1] who used 2-sulfanilamido-5-isopropyl-1,3,4-thiadiazole. Stimulated by this work, Loubatières[2] embarked on an intensive investigation of the compound, confirming its depressing effect on the blood sugar level. He showed that in dogs it could produce convulsions and irreversible changes in the nervous system analogous to those seen in prolonged insulin hypoglycemia, but that it was ineffective in the dog in which total pancreatectomy had been done. He suggested that the compound facilitated deposition of glycogen in the liver and adduced evidence pointing to a stimulation of insulin secretion.

In 1946, Chen and associates[3] reported hypoglycemia in normal rabbits given 2-sulfanilamido-5-cyclopropyl-1,3,4-thiadiazole and a paradoxical hyperglycemia in alloxanized animals so treated. The latter finding discouraged clinical trial of this material. Three German papers published simultaneously in 1955[4] described the hypoglycemic activity of an orally administered bacteriostatic agent, carbutamide (1-butyl-3-sulfanilylurea), designated BZ-55, in normal animals and normal human subjects and in diabetic patients. At about the same time, workers at the Hoechst laboratories in Germany reported similar results with a related but nonbacteriostatic compound, tolbutamide (1-butyl-3-*p*-tolylsulfonylurea), designated D-860, U-2043, and Orinase.[5]

The possibility that these substances might be effective in the treatment of diabetes mellitus promptly led to their use in extensive clinical investigations, at first in Europe and later in the United States and Canada. As of September, 1956, a total of 1,035 patients treated with sulfonylurea compounds have been reported in the literature available to us,[6] with favorable results in 60 to 80%. Actually, several times this number have received the drugs. Of the 1,035 patients, however, all but 30 appear to have been studied and evaluated by methods either incompletely described or, in our opinion, inadequate to permit unequivocal conclusions as to the efficacy of the treatment. In some instances, the patients had been hospitalized for tuberculosis or other bacterial diseases, so that amelioration of the diabetes might have been attributed to improvement in the infection. In others, patients with diabetes of short or unstated duration were used; since patients with diabetes often tend to improve when first brought under treatment, even though this be only dietary, it is difficult to be certain that any mitigation noted was the result of drug therapy. In still others, the effectiveness of the sulfonamide agent was judged by the ability of the patient to remain aglycosuric when insulin was withdrawn or dosage reduced. The pitfall here is that many older patients can tolerate the withdrawal of most or all of their injected insulin when they are brought into the hospital and placed on well-regulated diets. Finally, in many cases the period of observation before administration of the drug was too short to ensure that carbohydrate metabolism had reached a stable state against which the effect of treatment with sulfonamides could be properly measured.

Purpose

The present investigation was designed primarily to determine the effect of the sulfonylurea drugs, carbutamide and tolbutamide, on the levels of blood and urine sugar of a variety of diabetic patients under experimental conditions that would approximate the ideal as nearly as possible. A secondary aim, actually accomplished before the first, was to test the effect of these drugs in normal individuals in such a way that prolonged fasting and variations in fluid intake would not influence the results.

Procedure

The normal subjects (the majority of whom were male) were 11 individuals selected from the hospital staff and medical students. Each was subjected to three observations: 1. Prior to the administration of any drug, the blood sugar level was determined after an overnight fast and 200 cc. of milk was given immediately. Every two hours thereafter for eight hours, additional blood specimens were obtained and the same amount of milk was given. Regular meals were not ingested until the end of the experimental day. Ordinary activity was not curtailed. 2. Several days later, the entire procedure was repeated, this time with 2 gm. of carbutamide given as a single dose by mouth just before the first feeding of milk. 3. After at least one week, the same experiment was performed with use of tolbutamide. The fasting blood sugar level was determined again on the day after the administration of drug.

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Seven patients, including both young and old adults, with diabetes diverse in duration, severity, and lability were hospitalized primarily for experimental study on a metabolic ward for periods of 2 to 11 weeks. Except for one patient, previously adrenalectomized for metastatic carcinoma, none had complications that might influence diabetes. Twenty-four-hour specimens of urine for quantitative determination of glucose were collected, and capillary blood for glucose was obtained four times daily, with patients in the fasting state and three to four hours after each meal. Diets patterned after the home intake as revealed by diet records, and constant with respect to total calories, carbohydrate, protein, and fat, maintained the patients' weight, with no significant gain or loss.

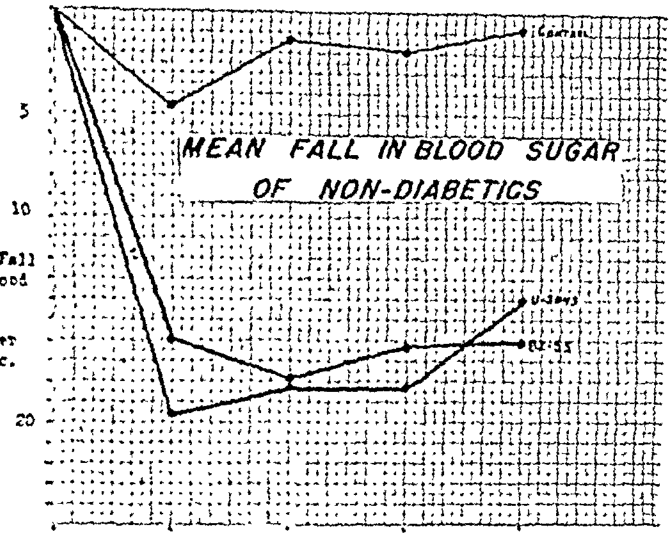

Fig. 1.—Mean fall in blood sugar level in nondiabetic subjects after single dose of either carbutamide or tolbutamide, contrasted with such depression in same individuals when no drug was given; 200 cc. of milk given every two hours during all experiments.

Observation prior to administration of the drug was prolonged until daily blood and urine sugar values seemed well stabilized or on an upward trend. Treatment with either drug was never initiated if blood or urine sugar level was decreasing. In some patients, insulin therapy was not completely discontinued but was reduced to a level that permitted significant hyperglycemia and glycosuria. The dose of insulin was then kept constant through the rest of the period of observation. The sulfonylurea drugs were given in divided doses three times daily except in case 5, in which they were given two times daily. Blood sulfonamide levels in the cases in which they were determined were in the generally accepted therapeutic range of 15 to 20 mg. per 100 cc.

Routine procedures carried out before and during administration of drugs included blood cell counts, complete urinalysis with a search for crystalluria, urea clearance, liver function tests (sulfobromophthalein [Bromsulphalein], cephalin and thymol flocculations, and determination of serum bilirubin value and of alkaline phosphatase value), basal metabolic rate (in some cases radioactive iodine [I^{131}] uptake and clearance), electroencephalograms, urinary 17-ketosteroids, and four-hour corticotropin-eosinophil depression tests.

Results and Report of Cases

Normal Subjects.—Of 11 normal subjects, 10 showed a maximal depression in the blood sugar level greater than 15 mg. per 100 cc. in response to one or both drugs. One failed to respond to either. In the entire group, the mean decrease in blood sugar level between fasting levels and each of the succeeding two-hour levels (e. g., 0 to 2, 0 to 4, 0 to 6, and 0 to 8 hours) was significantly greater when drug plus milk was given than when milk alone was given (fig. 1). Fasting blood sugar values the following morning were generally at predrug levels. Drowsiness and fatigue were noticed by some subjects, usually at a time when the blood sugar value was low. Neither drug was consistently superior to the other in causing hypoglycemia.

Diabetic Subjects.—The results in the seven patients with diabetes are given in the following case reports.

Case 1.—An obese woman aged 36, with diabetes of one year's duration, was observed on the metabolic ward for a total of 63 days. She had taken insulin for one year and, prior to hospitalization, had required approximately 40 units of isophane (NPH) insulin daily. Her weight was 83 kg. (183 lb.) and height, 156 cm. (61.5 in.). The diet contained 2,068 calories, with 202 gm. of carbohydrate, 90 gm. of protein, and 100 gm. of fat. Initially, the mean level of all blood sugar concentrations was approximately 200 mg. per 100 cc., with the patient receiving 20 units of isophane insulin daily. Twenty days were required to discern a mild downward trend in the glycosuria and hyperglycemia. For seven additional days prior to administration of carbutamide, the insulin dosage was decreased to 10 units daily and maintained at this level for the duration of the observations. On this regimen, 24-hour urine specimens showed glycosuria averaging 44 gm., and blood sugar levels were slightly higher than before. On the 28th day of hospitalization, carbutamide therapy was initiated, 3 gm. being given by mouth the first day, 2 gm. the second, and 1.5 gm. per day for several days thereafter. In an effort to achieve a more striking decline in blood sugar level, a daily dose of 3 gm. was resumed. Figure 2 shows the fall in average excretion of sugar from 44 to 12 gm. daily, and an average fall for all blood sugar values of 40 mg. per 100 cc. During a recovery period of 10 days without the drug, the mean blood sugar values climbed to near 200 mg. per 100 cc. and the mean daily excretion of glucose to 34 gm. A further mild fall in blood sugar level averaging 13 mg. per 100 cc. and a decrease in glycosuria from 34 to 10 gm. per 24 hours was accomplished with administration of 3 gm. of tolbutamide daily. Satisfactory control of this patient's diabetes was not obtained on either drug, and she was discharged from the hospital on a weight-reduction diet and regimen of 15 to 20 units of isophane insulin. Subsequent clinic visits revealed minimal glycosuria and nonfasting blood sugar levels under 125 mg. per 100 cc.

Case 2.—An obese woman aged 70, who had had diabetes for 16 years and had used insulin for 10 to 12 years, was observed on the metabolic ward for a total of 57 days. Prior to hospitalization, she had customarily taken 30 to 35 units of protamine zinc insulin daily. Her average weight before and during the period of study was 79.4 kg. (175 lb.), and her height was 157 cm. (62 in.). The diet contained 2,036 calories, with 170 gm. of carbohydrate, 96 gm. of protein, and 108 gm. of fat. Insulin therapy was discontinued after the third hospital day, and the patient was observed for another 12 days before administration of drugs. During the last five days of the control observation period, a

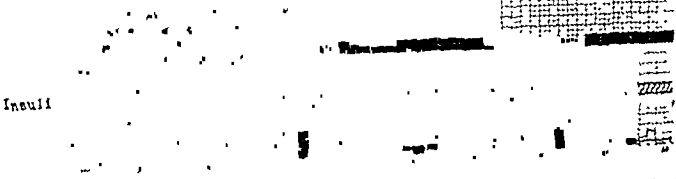

Fig. 2.—Chart of hospital course of patient in case 1. Total period of hospital observation, 63 days. In this and succeeding figures, days are indicated on horizontal axis. Horizontal lines are drawn through the blood sugar graph at levels of 100 and 200 mg. per 100 cc. Medication with sulfonylureas is indicated by solid bars. Insulin dosage is shown by hatched bars. Twenty-four-hour urinary glucose excretion is indicated by the open columns, while mean values for the periods indicated by the arrows are represented by solid columns. See text for details.

slight increase in glycosuria and hyperglycemia was noted. Tolbutamide therapy was started on the 16th day in doses of 3 gm. daily by mouth. On this regimen the average 24-hour excretion of sugar fell from 32 to 15 gm. and the mean blood sugar level from 262 to 237 mg. per 100 cc. A recovery period without the drug led to an average sugar excretion of 43 gm. per 24 hours and an increase in the mean blood sugar level to 286 mg. per 100 cc. Daily administration of 3 gm. of carbutamide was accompanied by a fall in urine sugar from 43 to 26 gm. and a fall in the mean blood sugar value to 251 mg. per 100 cc. Neither drug effected adequate control of this patient's diabetes (fig. 3), and she was sent home on a weight-reduction diet and a regimen of 10 units of isophane insulin daily. Nonfasting blood sugar values determined on return visits to the outpatient department have been 220 and 172 mg. per 100 cc.

Case 3.—An obese man aged 68, with diabetes of three months' duration, was observed in the hospital for 37 days, 23 of which were spent on the metabolic ward. He had never received insulin. His weight was 82.6 kg. (182 lb.) and height, 172.7 cm. (68 in.). The diet contained 1,994 calories, with 150 gm. of carbohydrate, 81 gm. of protein, and 100 gm. of fat. During the first eight days on the metabolic ward while no medicament was given, fasting and postprandial blood sugar values stabilized around a mean of 271 mg. per 100 cc. On the 23rd hospital day (9th on the metabolic ward) 3 gm. of carbutamide was given orally. The dose was reduced to 2 gm. the next day and then to 1.5 gm. for each succeeding day. The mean of all blood sugar values fell slightly to 260 mg. per 100 cc. Average 24-hour glycosuria, however, declined from 50 to 13 gm. The patient has continued to take 1.0 to 1.5 gm. of tolbutamide daily at home, with no glycosuria and nonfasting blood sugar values of 88 and 72 mg. per 100 cc.

Case 4.—A male, aged 24, who had had unstable diabetes for five years and had taken insulin for four years, was observed on the metabolic ward for 54 days. His weight was 68.5 kg. (151 lb.) and height, 172.7 cm. (68 in.). The daily dose of 45 units of isophane insulin used at home was changed to 40 units of protamine zinc insulin daily in the hospital, but excessive glycosuria, often over 100 gm. per day, made it necessary to resume therapy with 45 units of isophane insulin daily. The diet contained 2,384 calories, with 200 gm. of carbohydrate, 99 gm. of protein, and 132 gm. of fat. After 22 days of observation, 3 gm. of carbutamide was given daily by mouth for nine days. The mean of all blood sugar values rose from 199 to 241 mg. per 100 cc. and the 24-hour urine sugar from 34.2 to 58.1 gm. Carbutamide therapy was discontinued, and, without an intervening recovery period, tolbutamide in a dose of 3 gm. daily was given. On this regimen the mean blood sugar level was 206 mg. per 100 cc. and the mean daily sugar excretion was 49.8 gm. Both drugs were totally ineffective in controlling this patient's diabetes, and he was discharged on a regimen of 50 units of isophane insulin daily (fig. 4). Glycosuria continued at home, and a nonfasting blood sugar value was 245 mg. per 100 cc. The patient, maintained for several years and during hospitalization on therapy with phenobarbital and diphenylhydantoin (Dilantin) sodium because of epilepsy, failed to show any change in behavior or electroencephalographic pattern while under therapy with the sulfonylurea preparations.

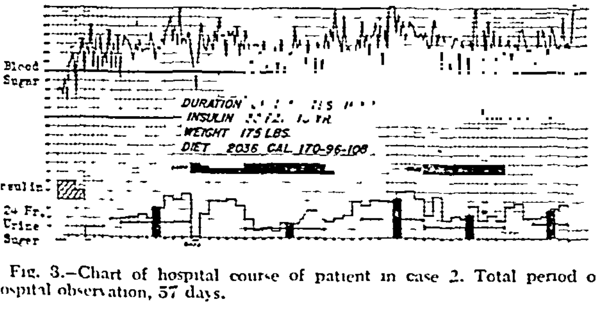

Fig. 3.—Chart of hospital course of patient in case 2. Total period of hospital observation, 57 days.

Case 5.—A woman aged 59, who had had diabetes for one year and who had used 25 units of isophane insulin daily for seven months, was observed on the metabolic ward for 17 days. Her weight was 71.2 kg. (157 lb.) and height 160 cm. (63 in.). This patient had undergone adrenalectomy about one year before the present study because of metastatic carcinoma of the breast. Her diet consisted of 1,592 calories, with 197 gm. of carbohydrate, 75 gm. of protein, and 53 gm. of fat. Prior to and during hospitalization, she was satisfactorily maintained on therapy of 50 mg. of cortisone daily. Insulin therapy was discontinued on admission. Blood sugar values for five days prior to the administration of 1 gm. of carbutamide daily averaged 149 mg. per 100 cc. The mean blood sugar levels on therapy with 1 gm. of carbutamide daily and finally with 2 gm. daily were 156 and 160 mg. per 100 cc. respectively. At no time, either before or during administration of the drug, was glycosuria present. Carbutamide therapy was discontinued when the patient was discharged from the hospital.

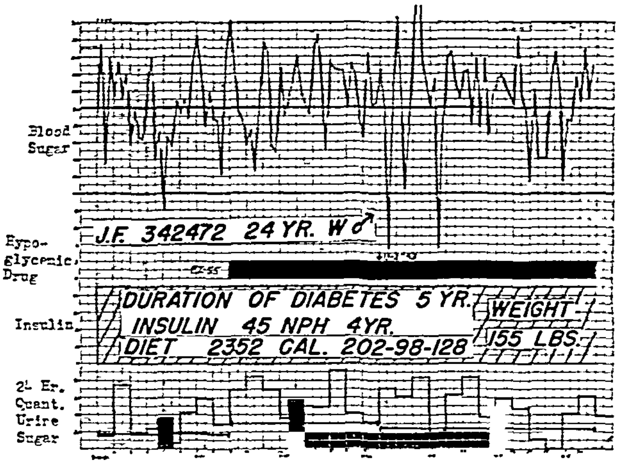

Fig. 4.—Chart of hospital course of patient in case 4. Total period of hospital observation, 54 days.

Case 6.—A moderately obese woman, aged 60, with diabetes of four years' duration and requiring approximately 50 units of isophane insulin daily, was observed in the hospital for 90 days, 76 of which were on the metabolic ward. Her weight was 66.7 kg. (147 lb.) and height 160 cm. (63 in.). Her diet contained 2,045 calories, with 204 gm. of carbohydrate, 98 gm. of protein, and 93 gm. of fat. Withdrawal of insulin for 12 days resulted in blood sugar values of above 240 mg. per 100 cc. at all times, and averaging 365 mg. per 100 cc. Glycosuria averaged 61 gm. daily. Administration of tolbutamide in doses of 3 gm. per day by mouth promptly abolished glycosuria and effected a striking fall in blood sugar to a mean value of 179 mg. per 100 cc. (fig. 5). During the second week of treatment, blood sugar levels fluctuated with rare exceptions between 120 and 140 mg. per 100 cc. Withdrawal of tolbutamide for one week resulted in a steady increase in blood sugar to levels of 280 and 300 mg. per 100 cc. and a mean daily excretion of sugar of 8.5 gm. Treatment with carbutamide (3 gm. per day) caused a fall in blood sugar to levels of 120 to 140 mg. per 100 cc. and again abolished glycosuria. The patient has continued to take 1 gm. of carbutamide daily since discharge from the hospital. No glycosuria has been noted and postprandial blood sugar values have been below 125 mg. per 100 cc.

Case 7.—A slightly obese woman, aged 47, with diabetes of one year's duration who had received insulin (10 units of isophane insulin) for two days only, was observed in the hospital without insulin for 56 days, 42 of which were spent on the metabolic ward. Her weight was 57.6 kg. (127 lb.) and height 150 cm. (59 in.). The diet consisted of 1,829 calories, with 174 gm. of carbohydrate, 83 gm. of protein, and 89 gm. of fat. After 17 days of observation, both blood and urine sugar values seemed stable, averaging 311 mg. per 100 cc. for the former and 50 gm. per day for the latter. Therapy with tolbutamide starting with 3 gm. the first day, 2 gm. the second, and 1.5 gm. daily for the next 17 days caused a slight fall in the mean blood sugar value from 311 to 282 mg. per 100 cc. and a more marked fall in the urinary sugar from 50.4 to 18.2 gm. A recovery period during which the patient received placebos lasted 12 days and resulted in a mean blood sugar value of 287 mg. per 100 cc. and a mean daily urinary sugar of 22.6 gm. Hospitalization could not be further prolonged, and the patient was started on therapy of 1.5 gm. of carbutamide daily at home. She has reported aglycosuria except on rare occasions, and postprandial blood sugar values have been 198 and 172 mg. per 100 cc. No weight loss has been noticed since discharge from the hospital.

Comment

All investigators[7] agree that the sulfonylurea compounds are rarely effective in the growth-onset type of diabetes but that they give good results in a high proportion of middle-aged and elderly obese patients with relatively mild diabetes of not more than a few years' duration. Although the small series of cases here presented is not entitled to statistical consideration, it may nevertheless be significant that striking results were observed in so few of the five patients in whom a favorable response was to be anticipated. Of these, one (case 5) was quite unresponsive to the drugs, two (cases 1 and 7) were only partially responsive so that diabetes could not be controlled with orally given medication alone, one (case 3) showed a partial response in the hospital but a much better one at home, while in only one (case 6) was an excellent therapeutic result obtained. The drugs were neither expected nor found to be effective in two patients, one (case 4) a juvenile diabetic and the other (case 2) an overweight, elderly woman with long duration of both diabetes and treatment with insulin.

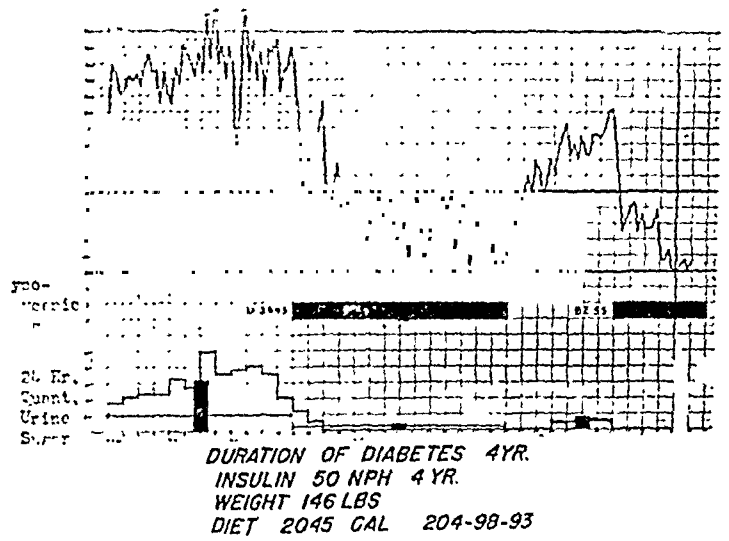

Fig. 5.—Chart of hospital course of patient in case 6. Total period of hospital observation, 90 days.

There may be two reasons for the discrepancy between the degree of success encountered in the present cases and that reported in the literature. The first is a difference in the rigidity of experimental conditions. Attention is called to the long period of observation that is sometimes necessary (e. g., case 1) before the diabetic state can be said to have become stabilized. In such cases a progressive decrease in glycosuria and insulin requirement occurs with no other treatment than exposure to a well-regulated hospital regimen and diet, and the premature administration of a new therapeutic agent can lead to erroneous conclusions. The second is a difference in criteria for "control" of diabetes. We regard good control as the maintenance of two-to-three-hour postprandial blood sugar levels of 150 mg. or less per 100 cc. and freedom from glycosuria, whereas in the majority of reported cases, chiefly from foreign sources, either no specific criteria are given[6] or it is stated that blood sugar values of 250 mg. or less per 100 cc. and glycosuria of less than 30 gm. per day constitute evidence of satisfactory control.[4c]

Contrary to experience with adrenalectomized animals,[7b] which are extremely sensitive to the hypoglycemic action of the sulfonylureas, the adrenalectomized diabetic woman of this series, maintained on 50 mg. of cortisone daily, exhibited no response to the drugs. Neither was she unduly sensitive to insulin. There was no apparent difference in effect on the blood sugar level between carbutamide and tolbutamide.

Side-effects were limited to leukopenia, which occurred in two cases. In one patient (case 2) the white blood cell count prior to treatment was 5,750 per cubic millimeter, with 46% granulocytes. After administration of 26 gm. of tolbutamide in 11 days, these figures were essentially unchanged. Administration of the drug was continued in the same dosage for 5 more days, this being followed by a recovery period of 10 days. At the end of the recovery period, treatment with carbutamide was started, and for the next nine days the patient received a total of 27 gm. Four days after withdrawal of carbutamide the white blood cell count was 3,300 per cubic millimeter, with 29% granulocytes, and two days later these values were 3,900 and 40% respectively. There were no symptoms. In a second patient (case 7) the pretreatment white blood cell count was 12,000 per cubic millimeter. At the end of a 21-day trial of therapy with tolbutamide (total dose 30 gm.), the white blood cell count was 10,000 per cubic millimeter. After a recovery period of 32 days, carbutamide was given on an outpatient basis, the patient receiving 13.5 gm. in 9 days. On the ninth day the white blood cell count was 4,300 per cubic millimeter. The drug was promptly withdrawn, and 22 days later the white blood cell count was 6,900 per cubic millimeter. There were no symptoms.

Neither clinical nor chemical hypoglycemia occurred in the absence of injected insulin, although such reactions have been reported elsewhere.[7b] Crystalluria was looked for but not observed. Treatment with the sulfonylurea compounds caused no change in tests of renal, hepatic, thyroid, adrenal, or cerebral function. Potentiation of barbiturate action, reported to occur in animals with relatively high dosage of carbutamide, was not apparent in the patient receiving anticonvulsive therapy for epilepsy.

The observations here reported throw no light on the mechanism by which the sulfonylurea compounds exert their hypoglycemic activity. Their ability to lower the blood sugar level in the normal subjects of this investigation confirms the experience of others and is in keeping with the hypothesis that the presence of insulin-producing tissue is necessary for this effect. There is experimental evidence pointing both to stimulation of the secretion or release of insulin and to inhibition of the breakdown of liver glycogen,[7b] but other modes of action have not been definitely excluded. It is still uncertain whether the effects on liver and pancreas are accomplished by physiological or innocuous means. Severe, even fatal, hepatitis due to drug intoxication has been reported,[7b] and the possibility of exhausting the already inadequate beta cells by prolonged stimulation, if this is what occurs, must be borne in mind.

Taken together, the rather unimpressive results obtained in this study, the paucity of knowledge concerning the mode of action of these compounds, and the relatively high incidence of side-effects, including some fatalities,[7b] make it probable that the usefulness of the sulfonylureas will be more limited than was originally anticipated and call for continued caution in their clinical application. They may, in selected cases, prove to fill a real need for patients who refuse to take insulin, for those who are allergic to it, and for those whose occupations render the use of insulin dangerous to themselves or others.

Summary

Of five diabetic patients selected on the basis of previous reports as being suitable candidates for treatment with carbutamide and tolbutamide and observed on a metabolic ward under carefully controlled conditions for long periods of time, one exhibited no response to the drugs, two had a partial response but still required insulin for proper control of the blood sugar levels, one had a delayed but ultimately satisfactory response, and one experienced a prompt and completely satisfactory response. The drugs were ineffectual in one patient with juvenile diabetes and in one elderly, obese patient who had taken insulin for many years. They produced significant lowering of the blood sugar level in 10 of 11 normal subjects. Leukopenia developed in two patients who had received first tolbutamide and then carbutamide.

It is suggested that the proportion of patients in whom these preparations can successfully replace insulin will be found to be smaller than previously reported if rigid experimental conditions are maintained and if strict criteria of diabetic control are followed. Use of the drugs will be most clearly justified in patients who will not, cannot, or should not take insulin. Until more is known about their mode of action and their long-term toxic effects, their distribution for general use should be delayed.

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This study was supported by grants from Eli Lilly & Company, Indianapolis, and the Upjohn Company, Kalamazoo, Mich.

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8 Footnotes 4*a*, 4*b*, 5, and 6*b*.

CLINICAL NOTES

EFFICACY OF PROMETHAZINE AND PYRATHIAZINE AGAINST ENTEROBIASIS

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and
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Recently Avery[1] reported a 97% cure rate in a group of 100 patients with enterobiasis (pinworm) who were given a single massive dose (125 mg.) of promethazine (Phenergan) hydrochloride. It is obvious that a therapeutic agent that is this effective, if it is nontoxic, offers great promise not only of curing individual patients but also of eliminating Enterobius infection from families, schools, and institutions for children. A previous study by Sadun and others,[2] who treated nine patients with this drug, reported a cure rate of only 44%. In view of Avery's remarkable results and the discrepancy in the results of the two studies, we, in order to verify the results, treated a group of children with promethazine under carefully controlled institutional conditions. A group of children were also treated with pyrathiazine (Pyrrolazote) hydrochloride, a compound closely related to promethazine. To confirm our results, we treated a number of mice infected with Syphacia obvelata, the mouse pinworm, with large doses of these two compounds and compared their therapeutic activity to that of piperazine hydrochloride, which is effective against pinworm in mice and man.[3]

Methods and Results of Treatment

Twenty-five children under 5 years of age, weighing from 27 to 52 lb. (12.2 to 23.6 kg.), were found by the cellophane-tape swab technique to harbor Enterobius vermicularis. They were immediately treated

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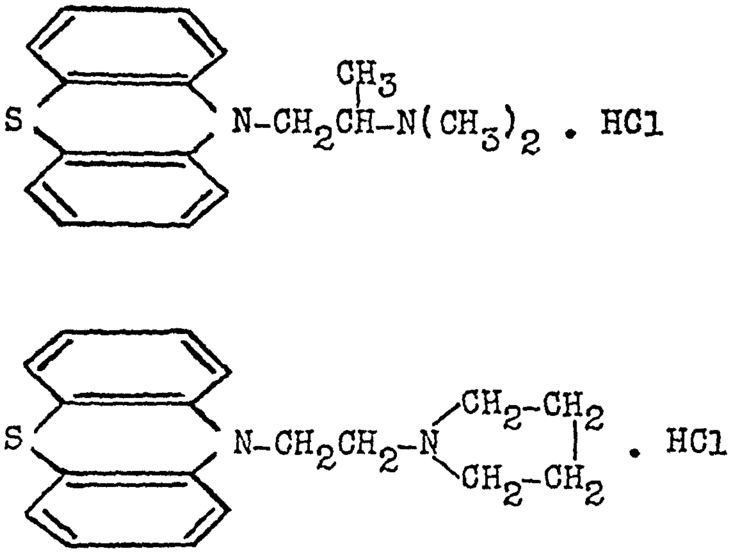
with either promethazine or pyrathiazine. A single 100-mg. or 125-mg. dose of the drug was administered in the evening before bedtime. No special dietary measures were employed. Seven to nine days after the treatment, cellophane-tape swabs were taken on the children for seven consecutive days. An Enterobius egg on any one of a patient's post-treatment swabs was considered indication of therapeutic failure. These swabs were all taken by us in the morning before the children were bathed. A series of mice experimentally infected with Syphacia obvelata were also given these two drugs, orally, in doses of 100 and 200 mg. per kilogram of body weight on two consecutive days. At autopsy their infection was compared to that of untreated control mice. The studies of Brown, Chan, and Ferrell [1] indicate that there is good correlation in the activity of chemotherapeutic agents against the pinworm of mouse and the pinworm of man.



Structural formulas of promethazine hydrochloride (*above*) and pyrathiazine hydrochloride (*below*).

Five of the 15 children treated with promethazine and 2 of the 10 children treated with pyrathiazine became free of Enterobius eggs after treatment, making the cure rates 33% and 20% respectively (tables 1 and 2). All the children except three became extremely drowsy as a result of therapy and slept heavily all night but were normally active on awakening in the morning. Three of the children treated with promethazine became very excited soon after administration of the drug and continued to be very active for several hours. One became so overactive that he was given a barbiturate in order to induce sleep. The mice given promethazine and pyrathiazine for two days at the rate of 100 and 200 mg. per kilogram of body weight harbored at autopsy approximately the same number of Syphacia as the control untreated mice (table 3). Infected mice given piperazine hydrochloride in these doses lost 65% and 80%, respectively, of their Syphacia.

TABLE 1.—*Effect of Promethazine in Fifteen Children with Enterobiasis*

Case No.	Weight, Lb.	Mg. of Drug	Post-Treatment Cellophane-Tape Swabs
1	31	100	—
4	27	100	+
6	28	100	+
17	32	100	—
42	35	125	+
28	42	125	+
18	36	125	—
11	40	125	+
64	35	125	+
70	42	125	+
75	43	125	+
80	25	100	—
84	27	100	+
87	27	100	+
96	39	125	—

Comment

Our results indicating that a single large dose of promethazine is relatively ineffective against enterobiasis do not confirm the studies of Avery, who reports a 97% cure rate. He administered a dose of 125 mg. to all his patients, "mainly children 3 to 12 years old," but also some adults. Our group of children were all under 5 years of age. Children weighing under 35 lb. (15.9 kg.) received 100 mg. of the drug, and those over 35 lb. received 125 mg. Although Avery does not present data on the weights of his children, the fact that adults and children up to 12 years of age received 125 mg. of the drug suggests that our therapeutic failures were not due to giving a smaller dose than he gave. Sadun and others,[2] who gave 90-160 mg. of promethazine to a group of nine patients, report a cure rate of 44%, which compares favorably with our 33% cure rate. These authors report that 21% of their untreated patients lost their Enterobius infections during the course of the therapeutic tests; 18% of our untreated control patients lost their infection. The failure of promethazine and pyrathiazine given in large doses to remove the pinworm Syphacia obvelata from mice confirms its ineffectiveness against the pinworm of man.

TABLE 2.—*Effect of Pyrathiazine in Ten Children with Enterobiasis*

Case No.	Weight, Lb.	Mg. of Drug	Post-Treatment Cellophane-Tape Swabs
32	32	100	—
35	30	100	+
38	27	100	+
23	36	125	+
52	42	125	+
55	35	125	+
63	52	125	+
71	35	125	+
72	38	125	+
78	44	125	—

TABLE 3.—*Effectiveness of Promethazine and Pyrathiazine as Compared with Piperazine Against Syphacia Obvelata in Mice*

		No. of Mice		Average Worm Burden		
Drug	Dosage, 2 Days	Treated Group	Control Group	Treated Group	Control Group	Reduction, %
Promethazine	100 mg./kg./day	6	5	107	120	11
Pyrathiazine	100 mg./kg./day	6	6	112	133	15
Piperazine	100 mg./kg./day	6	6	82	237	65
Promethazine	200 mg./kg./day	3	3	88	88	..
Pyrathiazine	200 mg./kg./day	3	3	100	88	..
Piperazine	200 mg./kg./day	6	5	24	115	80

Summary

Promethazine (Phenergan) hydrochloride administered at bedtime in a single dose of 100 or 125 mg. to 15 children, weighing 27 to 52 lb. (12.2 to 23.6 kg.), who were harboring Enterobius vermicularis resulted in a cure of 33% of them. Extreme drowsiness was experienced by 12 of these children, and 3 of them became extremely restless. Only 2 of the 10 children given 100 to 125 mg. of pyrathiazine (Pyrrolazote) hydrochloride lost their infection. These two compounds are likewise ineffective against Syphacia obvelata, the pinworm of mice, even when given in large doses.

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OBSERVATIONS ON BODY IMMERSED IN WATER FOR SIX YEARS

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There have been no previous cases documented in the medical literature with gross and microscopic findings on a body immersed in fresh water for six years. The purpose of this article is to describe in detail the findings in such a case. The legal aspects of this case are not considered here. The guilt or innocence of suspects is not properly the concern of medical authorities. A brief review of the background of this case is, however, necessary to indicate the circumstances that led to the discovery of the body and to provide substance for the statement that this body was that of the individual said to have been submerged in water six years before.

Two Italian partisans confessed to complicity in the murder of a U. S. Army officer in December, 1944. They claimed that he had been shot twice through the head with a Beretta pistol, after unsuccessfully being given potassium cyanide in his soup. They stated the body was then weighted in a sack and thrown into the cold waters of Lake Orta, on the borderland between Italy and Switzerland. On June 16, 1950, the waters of Lake Orta were dragged and a body was withdrawn from the location described by the two Italian confessors, together with material and clothes identified as the property of the U. S. Army.

Gross Morphology

The body, when taken from the water, was in a remarkable state of preservation. Eyewitness observers were quoted as saying that it looked like a *fantasmo* (ghost). I arrived to examine the body on June 19 three days after its withdrawal from the water. The body was placed in the cemetery of San Maurizio d'Opaglia, with no special refrigeration, under constant police surveillance. Decomposition was rapidly setting in. The skin and subcutaneous tissues, which were completely intact on first hitting the air, were now rapidly falling away from the body. Because of the delay in arrival of the two professors of legal medicine from the University of Turin, who were to jointly participate in the dissection, the autopsy was postponed an additional day. The grayish-white flesh fell away from the body to the degree that one-fifth of the body became denuded in the 24 hours under my personal observation. On June 20, 1950, with the arrival of Professors Busatti and Romanese of the Institute of Legal Medicine of the University of Turin, the autopsy was jointly begun.

Adipocere Formation

The external soft tissues on close analysis had undergone a peculiar grayish-white change. This process was referred to by the Italian authorities as saponification, a common finding in bodies that have been submerged in water. It is said to represent a change in the fatty acids of the subcutaneous tissues and occurs only after the body has been in water some time.[1] This process, called adipocere formation by American authorities, becomes complete one to one and one-half years after submersion, according to Gonzales and co-workers.[2] Since adipocere formation was complete in this body, it was agreed that the body must have been in the water at least one full year.

Identification of Body

Sex.—The area surrounding the external genitalia had sloughed off by the time the autopsy was performed. Fortunately, there remained intact, attached to the skull, an area of skin about the neck where a short stubbly beard was identified. Final conclusive confirmation of sex came from the identification of a prostate internally and an absence of internal female genitalia.

Race.—The hairs of the scalp were of a dark color and were removed for microscopic analysis by Professors Busatti and Romanese. The sparseness of pigment and the broken centrally placed medullary canal identified the hair as belonging to the body of a white person.[3]

Age.—Examination of the ends of the long bones showed that all the epiphyses were fused. The fusion of the metaphysis of the medial end of the clavicle and the epiphysis definitely placed the body as that of an individual over 25 years of age. Using the method of Krogman,[4] study of the degree of obliteration of the sutures of the skull and the changes in the ridges and grooves of the symphysis pubis placed the age of the body at death as in the middle or early 40's.

Conclusive Identifying Features.—The above-mentioned features all indicate the type of analysis to which unidentified bodies recovered from water are subjected. Specific identification on the above bases would certainly be impossible, yet the body was identified as belonging to a white male in his middle or early

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and pyrethiazine for two days at the

[illegible] who had definitely been submerged over one full year at the least. Since the body was specifically identified by the suspects, a study for critically identifying features was undertaken, and three such features were found.

Height: The identified Army officer was a tall man who measured 6 ft. 2 in. (188 cm.) in his bare feet. This precisely matched the height measured on the corpse.

Funnel Chest Deformity: The officer was known to have a pectus excavatum. This was noted upon his medical examinations, and an earlier photograph of him stripped to the waist showed its distinct presence. Autopsy of the body showed a distinct depression of the lower part of the sternum.

Dental Record: A careful analysis of the teeth of the corpse and their fillings was prepared by Prof. Alexander Tardy, an anthropologist working for U. S. Graves Registration. This record agreed closely with that of the officer's private dentist and the record of subsequent fillings done while he was in service.

Cause of Death.—Two bullets were found in the skull of the deceased. The ballistic data indicated that there was close enough correspondence between their riflings and the riflings of the Beretta supplied by the suspects when they confessed. Complete correspondence could not be ascertained because of deformity of the bullets in striking the bony structures. One bullet was lodged in the right occipital lobe after entering the left parietal region. The other was lodged in the base of the skull to the right of the foramen magnum. The second bullet pointed upward, forward, and medial- rd. On the basis of the poor penetration of the bul- he Italian medicolegal experts estimated that the s must have been fired from some distance. This ally indicated that the wounds were not self- icted. Further corroboration came from the location f the wounds. First, the left parietal region is a highly unusual site for suicide by a right-handed man. The bullet that was fired from behind had lodged in such a manner that the murder weapon could not have been held by the deceased. Toxicologic analysis of the stomach contents failed to disclose evidence of any poison.

Microscopic Data

The above information, I feel, definitely identifies this body as that of the Army officer who was dropped into Lake Orta in December, 1944, and was dragged out in June, 1950. Accepting this evidence as adequate for identification of the body, the morphological changes that were found have considerable interest from a medical point of view.

On opening the chest and abdomen, I did not know whether we would find a completely unidentifiable mass of protoplasm or a reasonable facsimile of a human being. As might have been predicted from the gross external examination of the body, the internal organs were in an amazingly intact state of preservation. The heart, lungs, stomach, intestines, liver, spleen, pancreas, adrenals, kidneys, bladder, and prostate were readily and simply identified. Their size, shape, consistency, and location appeared like those of a body freshly examined. Sections of each of these organs were placed in 10% formaldehyde solution (Formalin) for preservation and were then forwarded to the Fourth Medical Laboratory in Heidelberg, Germany, for the preparation of histological sections. After an appropriate period necessary for adequate fixation and staining, the slides were returned to us. The staining technique used was the standard hematoxylin and eosin method. At this point, the most amazing medical feature of the case emerged. Examination of the slides under the microscope showed a complete dissolution of histological structure, so that in no case could any organ be definitely identified.

It is interesting to speculate on what changes occurred in the tissue matrix to permit gross identification of organs as to size, shape, and location, while completely wiping out their histological structure. It would seem reasonable to run experiments with dead tissue immersed in water from different rivers and lakes for different periods of time to determine if a definite pattern exists for the histological disintegration of tissue. It would be of interest to discover whether an orderly pattern of disorganization takes place, which organs are first attacked and to what degree, and whether different natural waters have selective effects. The compilation of such data might well permit the prediction of time of immersion of a body in water in cases where the identification of the corpse is not as easy as in this case.

Summary and Conclusions

Gross and microscopic studies were made of a body immersed in fresh water for six years. There was a peculiar association of complete preservation of the gross structures of the internal organs with complete disintegration of the histological pattern. Experiments should be done with tissue obtained post mortem immersed in water for different periods of time to discover the time and rate at which such histological disintegration takes place and its fashion so that this disintegration may be used as a method for determining length of time of submersion of unidentified bodies.

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Geriatric Surgery.—The defeatist attitude toward geriatric su gery common among physicians and the general public unjustified and should be dispelled. The results of surge old age can be gratifying, and necessary surgery should withheld on the score of age alone. Much remains to be the prevention of trauma in old people and in stressing th astrous results of delay in diagnosis of both malignant di and acute abdominal conditions. Early diagnosis and treat are every whit as important as in younger patients. Fo surgeon emphasis must be laid on the prevention of compli tions. Above all shock must be averted by careful supporti measures, by good anesthesia, and by careful, atraumatic sur- gery. Given these, the outlook for the elderly surgical patient i encouraging.—*Jean Limbosch, M.D., Experiences with More Than One Thousand Elderly Surgical Patients, A. M. A. Archives of Surgery*, July, 1956.

COUNCIL ON FOODS AND NUTRITION

Report to the Council

The following paper was presented at the symposium "Some Inorganic Elements in Human Nutrition," in Nashville, Tenn., April 4, 1955. This symposium was sponsored jointly by the Nashville Academy of Medicine, the Vanderbilt University School of Medicine, and the Council on Foods and Nutrition. This report is the fourth of the series, the others of which appeared in THE JOURNAL *April 21, June 9, and Sept. 15, 1956.*

PHILIP L. WHITE, SC.D., *Secretary.*

THE METABOLIC ROLE OF ZINC

Bert L. Vallee, M.D., Boston

The metabolic role of zinc has been studied for many years,[1] but it was not until 1940 that Keilin and Mann offered the first concrete explanation of its mode of action.[2] They showed that the enzyme carbonic anhydrase contains 0.33% zinc as a part of its molecule and that zinc is essential to the elimination of carbon dioxide. Thus, zinc and iron have been shown to be components of two proteins, hemoglobin and carbonic anhydrase, pivotal from the point of view of respiratory gas exchange. This work foreshadowed the identification of zinc as a participant in other important enzymatic reactions. Information concerning the physiological and biochemical role of zinc in plant and animal metabolism has been accumulated and reviewed.[3] Therefore, to avoid unnecessary duplication, this paper will cover some of the salient facets of the physiological, biochemical, and clinical implications of zinc metabolism, emphasizing recent observations.

Physiology

The usual human intake of zinc is 10 to 15 mg. per day. The element is excreted mainly through the intestines; the feces contain about 10 mg. and the urine about 0.4 mg. per day.[4] The zinc content of human organs varies from 10 to 200 mcg. per gram of wet weight of tissue. Most organs, including the human pancreas, contain about 20 to 30 mcg. per gram. Contrary to some statements, the pancreas does not have unusually large concentrations of zinc although it has been shown that the islet tissue of fish is rich in the element, containing 100 to 1,000 mcg. per gram of fresh tissue.[5] No significant difference has been detected in the zinc content of the pancreas in normal and diabetic patients. The liver, voluntary muscles, bladder, and bones of man hold 60 to 180 mcg. of zinc per gram of fresh tissue and the normal prostate 859 ± 96 mcg. per gram of dry weight.[6] Outstanding in their content of zinc are the tissues of the eye. From 500 to 1,000 mcg. per gram has been found in the retina and as much as 5,000 mcg. of zinc per gram in the iris of fish and mammals other than man.[7]

The total amount of zinc in the human body has been estimated to be 2 gm. Apparently no tissue stores zinc preferentially. Human whole blood contains about 900 mcg. of zinc per 100 ml.[8] No serum zinc levels probably range from 80 to 170 m per 100 ml.; Vikbladh reports average and norr values of 124 ± 16 mcg. per 100 ml.[9] Normal erythr cytes contain 1.44 mg. of zinc per 100 ml. of pack red blood cells. Three per cent of all zinc in hum blood is found in leukocytes, which contain 0.032 mc of zinc per million cells.[8] Blood zinc concentratio do not exhibit seasonal or diurnal variations, nor d they differ between the sexes. They are normal i diabetics.[9]

The distribution of radioactive zinc (Zn^{65}) wa studied in the mouse and dog.[10] In both animals, th liver contained the largest fraction of the injecte dose of Zn^{65} early in the experiment. The most rapi uptake was observed in the liver, kidney, pancreas and pituitary; least activity was found in erythrocytes brain, skeletal muscle, and skin. Red blood cells and bone were the only tissue components to accumulate zinc gradually. This isotope has been detected in dogs and humans for as long as eight months or a year after its administration.[11] With the injecting of radioactive zinc into a pregnant dog, the passage of the isotope across the placenta into all of seven puppies has been demonstrated. The total stable zinc content of the tissues of these animals was similar to that of adults. The ratio of radioactive zinc to total zinc in three of the animals killed at intervals during the first postnatal week showed a redistribution of the isotope in all organs. There was a decrease in concentration in the extremities and a rise in concentration in the viscera.[11]

Zinc deficiency in animals was studied as early as 1922,[12] but the first successful experiments were reported in 1934 and 1935.[13] Todd, Elvehjem, and Hart found that the growth of rats deficient in zinc was only one-third that of normal ones; the zinc-deficient animals required 52% more ration to gain a gram in weight.[13a] Their fur softened and turned black to gray in six to seven weeks. Administration of adequate amounts of zinc subsequent to the termination of the deprivation experiment caused two animals to return to a normal appearance. The rats considered deficient in zinc received 22 mcg. of zinc per day. The feeding of 30 mcg. of zinc per day produced marked improvement; 40 mcg. of zinc per day completely eliminated manifestations of zinc deficiency. The normal controls received 300 mcg. of zinc per day.

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Studies of the carbohydrate metabolism in these animals deficient in zinc showed a delayed and irregular glucose tolerance curve, with normal fasting blood sugar levels and normal liver glycogen values. These findings suggested delayed absorption of glucose from the gastrointestinal tract.[11] These rats had a low plasma protein level and a definite reduction of pancreatic amylase and proteolytic activity, which could not be restored to normal by the addition of zinc, in vitro or in vivo. Because similar results had been obtained in magnesium deficiency, however, the change was considered the result of general debility.[15] Zinc had no effect on crystalline pepsin and trypsin in vivo. Although no changes in bone phosphatase were found, intestinal phosphatase activity in rats deficient in zinc was considerably decreased. In all the animals the zinc content of the soft tissues was normal, but that of the bone was lowered.[16]

Hove, Elvehjem, and Hart studied carbonic anhydrase activity in animals deficient in zinc. Although a slight anemia was found, there was no significant lowering of the enzyme activity in erythrocytes.[17] Plasma uric acid levels of the rats deficient in zinc were found to be doubled. Carbohydrate, fat, protein, or nucleoprotein content of the diet did not influence the course of zinc deficiency, and the uric acid blood findings were not reversed until five weeks after zinc had been added to the diet. This increased uric acid content seemed to be caused by increased uric acid formation, rather than by lack of destruction, since uricase activity was completely normal.[18]

Zinc and Hormones.—The crystallization of insulin as a zinc salt by Fisher and Scott led to the belief, now widely held, that zinc is an integral part of the insulin molecule. This belief persists in spite of the fact that nickel, cobalt, and cadmium can be used instead of zinc in the crystallization.[19] Actually, Fisher and Scott never stated that zinc was an integral part of the insulin molecule; they reported that these metals and insulin combined in a constant ratio. For zinc, the percentage in combination was 0.52, for cadmium 0.77, for cobalt 0.44; these percentages were not changed by recrystallization. Moreover, amorphous insulin is as active physiologically as is crystallized insulin, and there is little convincing evidence at present that zinc and insulin must combine in vivo to form an active compound. There is far more zinc in the pancreas than would be necessary for insulin activation, and some of it is now accounted for by carboxypeptidase.[20]

Understanding of the interrelation between zinc and insulin has been complicated further by the finding that 0.02% zinc, added to insulin as the chloride, reduces the immediate activity of the hormone by 40%, though the over-all potency of the hormone is not affected if enough time is allowed for it to act. No such effect is obtained when zinc and insulin are injected separately; precipitation of insulin from a zinc insulin solution with trichloroacetic acid restores its initial properties. Nickel causes the same changes.[21]

The subject of the relationship of zinc to the physiology of the pancreas in general and to that of insulin in particular has been reopened recently, based on the histochemical studies of Okamoto.[22] Employing a nonspecific technique based on the use of diphenylthiocarbazone (dithizone), Okamoto found variable amounts of zinc in the islands of Langerhans. With this agent, Kadota[23] produced diabetes in rats; he presumed that dithizone combined with the zinc of insulin to cause this experimental diabetes. On the basis of similar data, Maske concluded that insulin is physiologically stored as a zinc complex in the islands of Langerhans.[24] Other workers[26] found that the experimentally induced diabetic pancreas contained less zinc[25] and Zn^{65} than did its normal counterpart.[26] McIsaac has employed autoradiography to distinguish between the uptake of Zn^{65} by acinar and islet cell tissue of the pancreas.[27] He found that Zn^{65} concentration of the islet cells remained stable throughout the experimental period, whereas the concentration of acinar tissue, initially high, decreased with redistribution and excretion of Zn^{65}. He estimated that 50% of the injected Zn^{65} is excreted rapidly and 42% enters a "compartment" from which the loss is very slow. Zinc in islet tissue, McIsaac believes, is of the latter moiety. No conclusions were drawn concerning the postulated association of zinc with insulin in vivo.

Weitzel analyzed quantitatively the islet tissue of fish for both insulin and zinc and found them to parallel one another.[5] The zinc content varied from 100 to 1,000 mcg. per gram of fresh islet tissue, depending upon the physiological state of the animal. Much more zinc is present than can be bound to insulin. Histochemical evidence advanced in support of the hypothesis that zinc and insulin are associated in vivo is tenuous at best because the method employed is not specific for zinc. McIsaac, whose data are based on Zn^{65} studies, makes the most persuasive case in favor of a zinc-insulin complex,[27] but he is careful not to extrapolate beyond the evidence presented. The debate on zinc-insulin interaction continues without the achievement of a conclusive settlement.

The relationship between zinc and the activation of hormones needs further clarification, in view of the fact that zinc has been said to influence hormones other than insulin.[28] It has been reported that the addition of zinc to hypophysial gonadotropic extracts augments their effect greatly, as judged by production of estrus and changes in the uterus. Similar effects of copper and zinc on follicle-stimulating hormones and luteinizing hormone have been noted in the rat.[28] On the other hand, the addition of zinc to equine gonadotropin decreases its activity. The physiological significance of these findings is not clear.

Zinc and Porphyrins.—It seems certain that a zinc uroporphyrin exists. Some investigators have found the zinc complex of the Waldenström uroporphyrin to be a constant constituent of the urine and feces in cases of intermittent, acute porphyria.[29] Urinary excretion alone seemed to be the rule in the acute, intermittent cases. In fact, the occurrence of the zinc porphyrin complex is characteristic of this type of porphyrinuria, whereas in the congenial type the porphyrin is usually excreted in a free state.[30] In the latter cases, a zinc uroporphyrin is found in the liver. A zinc coproporphyrin, which has also been described,[30a] has been found in cases of lead poisoning,[31] and its presence in the urine of victims of acute rheumatic fever has been confirmed.[30a]

of 10 to 12 years.[47] Certain intractable types of cyanosis and dyspnea of infants at birth have been attributed to very low carbonic anhydrase activity and may be benefited by transfusion of adult red blood cells. A decrease of 50% in the concentration of zinc in the whole blood of Chinese suffering from protein deficiency, acute and chronic beriberi, and pellagra has been reported. No separate values for erythrocytes and serum were obtained, and no hematological data were given.[48]

Changes in Leukocyte Content.—Marked increases of leukocyte zinc have been seen in patients with anemias refractory to all therapy and accompanied by leukocyte counts below 2,000 per cubic millimeter.[49] The zinc concentration of leukocytes in acute and chronic lymphatic and myelogenous leukemia is decreased to 10% of the normal value. With successful therapy, the zinc concentration returns to normal. Administration of zinc salts intravenously fails to raise the leukocyte zinc concentration or to influence the course of the disease. The phenomenon is apparently independent of the maturity of the cells.[50]

Changes in Urine Content.—The normal zinc content of urine, 0.3 to 0.4 mg. per 24-hour volume, has been found to rise sevenfold to 2.1 mg. per 24-hour volume in patients with albuminuria.[4]

Comment

Disturbances of zinc metabolism have been noted in a variety of conditions; their detection, while supplementary to established diagnostic procedures, does not replace these procedures. A great deal more experience is necessary before studies of zinc can be assigned a decisive diagnostic role. At present, there is no known therapeutic role for zinc in systemic disease.

Because of space limitations, the bibliographic references have been omitted from THE JOURNAL and will appear in the author's reprints.

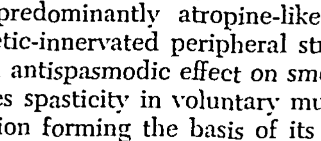
COUNCIL ON PHARMACY AND CHEMISTRY

NEW AND NONOFFICIAL REMEDIES

Monographs and supplemental statements on drugs described here and in subsequent editions of New and Nonofficial Remedies are based on the evaluation of available scientific data and reports of investigations. Applicable commercial names for preparations of evaluated drugs are listed at the end of monographs and parenthetically in the text of supplemental statements; additional commercial names of which the Council is informed will be included with subsequently published supplemental statements and annual editions of New and Nonofficial Remedies.

H. D. KAUTZ, M.D., *Secretary.*

Procyclidine Hydrochloride.—1-Cyclohexyl-1-phenyl-3-pyrrolidino-1-propanol hydrochloride.—The structural formula of procyclidine hydrochloride may be represented as follows:



Actions and Uses.—Procyclidine hydrochloride, a synthetic aminopropanol, is related in chemical structure and pharmacological action to cycrimine hydrochloride and trihexyphenidyl hydrochloride. Thus, the drug exerts predominantly atropine-like actions on parasympathetic-innervated peripheral structures and a pronounced antispasmodic effect on smooth muscle. It also relieves spasticity in voluntary muscle groups, the latter action forming the basis of its clinical use.

Procyclidine hydrochloride is employed for the symptomatic treatment of paralysis agitans (Parkinson's disease). It is as effective for this purpose as the hydrochloride salts of cycrimine and trihexyphenidyl. Thus, the drug is more useful for reducing muscle rigidity in postencephalitic Parkinsonism than in the arteriosclerotic or idiopathic types of the disease. Effect on tremor is variable; in general, tremor is reduced, although in some severely spastic cases this symptom can become exaggerated as rigidity is relieved. For patients with severe tremor and advanced rigidity, the combination of procyclidine with other antispastic drugs may be advisable.

On the basis of laboratory studies and clinical experience thus far, it would appear that the toxicity of procyclidine hydrochloride is not significant. Side-effects are typical of those produced by parasympatholytic drugs and include dryness of the mouth, mydriasis, lightheadedness, and disorientation. Gastric upsets are also produced occasionally. The frequency, duration, and intensity of these side-effects are chiefly a function of dosage and at clinical levels consist usually only of dryness of the mouth. The drug should be administered cautiously to all patients with glaucoma, tachycardia, and urinary retention.

Dosage.—Procyclidine hydrochloride is administered orally. Dosage is variable depending on the age of the patient and the cause of the disease. In general, younger patients and those who have had encephalitis require and tolerate a higher dosage than do older patients and those with arteriosclerotic or idiopathic Parkinsonism. The usual initial dose is 7.5 mg. per day administered in three divided doses after meals. This may then be gradually increased to 15 to 30 mg. per day. Doses as high as 45 to 60 mg. daily have been employed, usually without undue side-effects.

Applicable commercial name: Kemadrin.

Burroughs Wellcome & Company, Inc., cooperated by furnishing scientific data to aid in the evaluation of procyclidine hydrochloride.

Boston, Dr. Marcia S. Hays, bureau of crippled children's service, *California Department of Public Health*, Berkeley, Calif., Dr. Pearce Bailey, National Institute of Neurological Diseases and Blindness, Bethesda, Md., and Dr. George G. Deaver, Institute of Physical Medicine and Rehabilitation, New York University-Bellevue Medical Center, New York, will participate in presentation of "Medical Progress and Prospects." The afternoon session on "Cerebral Palsy Needs and Services in Illinois" will include presentation of "What We Parents Want for Our Cerebral Palsied Children" by a parent; and "What We Cerebral Palsied Adults Need" by a cerebral palsied adult. "Illinois State Programs for the Cerebral Palsied" will be discussed by Dr. William A. Tomlinson, division of services for crippled children, University of Illinois College of Medicine, Chicago; E. C. Cline, Ph.D., Illinois Division of Vocational Rehabilitation, Springfield; Miss Jane Bull, Illinois Commission for Handicapped Children; Willard Couch, Illinois Department of Public Welfare; and Ray Graham, Division of Exceptional Children, Illinois Office of Public Instruction. There will be no registration fee.

MISSOURI

Personal.—Dr. Henry C. Sweany, formerly director of laboratories and research at the Chicago Municipal Tuberculosis Sanitarium and now director of research, pathology, and allied sciences, Missouri State Sanatorium, Mount Vernon, recently received the medal awarded annually by the American College of Chest Physicians for outstanding contributions in chest pathology.—Dr. Noah D. Fabricant, clinical assistant professor of otolaryngology, University of Illinois College of Medicine, Chicago, will speak on "Diagnosis and Treatment of Ear, Nose, and Throat Diseases" in a Symposium on Office Procedures at the Muehlenbach Hotel, Kansas City, Mo., Nov. 11, under the auspices of the Wyandotte chapter of the Kansas Academy of General Practice, the Greater Kansas City chapter of the Missouri Academy of General Practice, and the Lederle Laboratories.

NEW JERSEY

Beling Lecture.—The New Jersey Neuropsychiatric Association announces the 10th annual C. C. Beling Lecture at the Veterans Administration Hospital, East Orange, Nov. 14. "Disorders of Homeostasis in Nervous and Mental Diseases" will be the subject of Dr. Warren S. McCulloch of the Research Laboratory of Electronics, Massachusetts Institute of Technology, Cambridge, Mass.

Albee Memorial Lecture.—The fifth annual Dr. Fred H. Albee Memorial Lecture will be presented at the Kessler Institute for Rehabilitation, Pleasant Valley Way, West Orange, Nov. 10, 2 p. m., by Dr. Francis J. Braceland, medical director of the Institute of Living, Hartford, Conn. His topic will be "The Role of Psychiatry in Rehabilitation." The program will include significant case presentations by members of the institute medical staff. Members of the medical profession and allied rehabilitation, health, and welfare professional personnel are invited to attend.

Meeting of Alumni Association.—The ninth annual meeting of the Alumni Association of the Jersey City Medical Center will be held at the hospital, Nov. 14. A tour of the medical center and the Seton Hall College of Medicine and Dentistry will be conducted in the morning, and a scientific program, including exhibits, symposiums, and case presentations will be given in the afternoon. Dr. Louis A. M. Krause, clinical professor of medicine, University of Maryland School of Medicine, Baltimore, will be the main speaker at the evening dinner.

NEW YORK

Symposiums on Development of Physiological Thought.—The State University of New York College of Medicine at New York City, Brooklyn, will offer a series of symposiums dealing with the historical development of physiological thought in the medical sciences at its new Basic Sciences Building, 450 Clarkson Ave., Brooklyn, during the coming academic year. The first symposium will consist of the following presentations:

Nov. 13, Dependence of Medicine on Basic Scientific Thought, Owsei Temkin, associate professor of the history of medicine, Johns Hopkins University School of Medicine, Baltimore (4:30-5:30 p. m.). Physiology and the Recurrent Problem of Vitalism, Iago Galdston, executive secretary, committee on medical information, New York Academy of Medicine, New York City (8-9 p. m.).

Nov. 14, Structural Basis of Function and Anatomical Reasoning in Physiological Thought, Lloyd G. Stevenson, associate professor of the history of medicine, McGill University Faculty of Medicine, Montreal, Canada (4:30-5:30 p. m.). Development of Ideas Relating the Brain with the Mind, Horace W. Magoun, Ph.D., professor of anatomy, University of California at Los Angeles School of Medicine (8-9 p. m.).

Nov. 15, Development of Knowledge of the Cardiovascular System, Chauncey D. Leake, Ph.D., assistant dean and public information officer, Ohio State University College of Medicine, Columbus, Ohio (4:30-5:30 p. m.).

New York City

Harvey Lecture.—The third Harvey Lecture in the 1956-1957 series will be delivered Nov. 15, 8:30 p. m., at the New York Academy of Medicine, 103rd Street and Fifth Avenue, by Erwin Chargaff, Ph.D., professor of biochemistry, Columbia University College of Physicians and Surgeons, on nucleic acids and nucleoproteins.

Salmon Lectures.—The 24th series of the Thomas William Salmon Lectures will be delivered Nov. 15 by Horace W. Magoun, Ph.D., professor of anatomy, University of California at Los Angeles School of Medicine. Dr. Magoun, visiting scientist at the National Institute of Mental Health in Bethesda, Md., will discuss "The Waking Brain: The Role of the Reticular System in Wakefulness and Behavior." Dr. Magoun's current research is directed to contemporary and historical aspects of the relations of the mind with the brain. The lectures will be given at 4:30 and 8:30 p. m. in Hosack Hall of the New York Academy of Medicine.

School Health Study.—The Welfare and Health Council of New York City has announced the launching of a complementary mental health study as part of its three-year school health survey. According to Dr. Ray E. Trussell, the recently appointed chairman of the survey advisory committee, the survey is being conducted with the co-sponsorship of the New York City Board of Education and Department of Health, with support in part by a $160,000 grant from the U. S. Public Health Service. It will seek to determine the effectiveness of the city school health service in placing children with health problems under care and in improving methods of referral to facilitate proper and timely treatment. Formulation and design of the new mental health program will be undertaken by Dr. Stella Chess, associate clinical professor in psychiatry at Flower and Fifth Avenue Hospitals and coordinating psychiatrist at the Northside Center for Child Development. Dr. Lauretta Bender, research director of the New York State Department of Mental Hygiene, will serve as principal consultant and Dr. William C. Spring Jr. as project director. The school health survey entails a core study of elementary and junior high-school students whose health and academic records will be reviewed. Selected groups of this sample will be given health examinations and checked through interviews with members of the family, teachers, principals, nurses, and others who are concerned with child health. The program is being undertaken in public and parochial schools in the city, including populations of high, medium, and low socioeconomic standing, with due consideration for ethnic, educational, and other characteristics.

NORTH CAROLINA

Grant in Geriatrics.—The psychiatry department of Duke University School of Medicine, Durham, N. C., has been awarded a $211,000 research grant by the National Institute of Mental Health for a five-year continuation of research on the effect of aging on the physiological and psychological functioning of elderly people. Dr. Ewald W. Busse, chairman, psychiatry department, is chief investigator for the project. Working with him will be a research team composed of some 16 faculty members, research workers, and graduate students, who will continue the work initiated in 1950 by Dr. Busse and his associates at the University of Colorado School of Medicine in Denver. The project's primary goal is to provide a better understanding of the changes that take place in normal people as they become older. An annual budget of $44,200 has been set up. Research procedures will include study of social and medical histories, psychiatric evaluation, physical examinatio vatio controlled social situations, and psychologi

OHIO

Traineeships in Cardiovascular Disease.—A cardiovascular disease training program for young physicians has been inaugurated by Frank E. Bunts Educational Institute, teaching unit of the Cleveland Clinic. Two-year traineeships oriented toward research and academic practice are available to physicians who have completed approved internships and at least two years of approved residency in internal medicine or pediatrics. For eight months of the traineeship period the participants will study cardiovascular-renal disease in the research division of the institute. The remaining 16 months will be divided equally between study of general cardiology and pediatric and surgical cardiology in the division of medicine. In each field the trainee will undertake a specific research project. Responsibility for the training in the research division is in the hands of Drs. Irvine H. Page, Arthur C. Corcoran, and Harriet P. Dustan. In the division of medicine the responsibility is shared by Drs. A. Carlton Ernstene, William L. Proudfit, and F. Mason Sones Jr. Information may be obtained from the program coordinator, Dr. Charles L. Leedham, Frank E. Bunts Educational Institute, 2020 E. 93rd St., Cleveland 6.

PENNSYLVANIA

Alumni Association Day.—The Medical Alumni Association of the University of Pittsburgh will hold its sixth annual Scientific Day in the Mellon Institute Auditorium, Pittsburgh, Nov. 16. At 10 a. m. Dr. George Crile Jr., Cleveland, will discuss "Factors Influencing the Dissemination of Cancer" which will be followed by "The Definition of Inoperability of Cancer" by Dr. George T. Pack, New York. Luncheon will be held at Webster Hall. The afternoon session will open at 3 p. m. with "Use and Abuse of Steroids in Therapy" by Dr. William A. Sodeman, Columbia, Mo., and will be followed by the presentation of "The Pathogenesis of Fever" by Dr. W. Barry Wood Jr., Baltimore. Scientific exhibits will be on display from 2 to 5 p. m. A cocktail hour will be held at 5 p. m.

Philadelphia

Psychiatrists Give Award to Dr. Roche.—At the annual meeting of the American Psychiatric Association, Dr. Philip Q. Roche, assistant professor of psychiatry, University of Pennsylvania School of Medicine and University of Pennsylvania Graduate School of Medicine, received the $1,000 Isaac Ray Lectureship award, given annually to a lawyer or psychiatrist for contributing importantly to better understanding between the two professions. Dr. Roche, who was at one time chairman of a joint commission of the Philadelphia County Medical Society and the Philadelphia Bar Association, was largely responsible for the "Pennsylvania Plan for Intramural Training in Penal Psychiatry," which, supported by the Commonwealth Fund, provided fellowships for training physicians in penal psychiatry at Eastern State Penitentiary in Pennsylvania. A founding member of the Pennsylvania Psychiatric Society, Dr. Roche served as its president in 1952-1953.

Cited for Aiding the Handicapped.—Dr. Albert A. Martucci, a past-president of the Philadelphia County Medical Society and during the past 13 years chairman of the commission on physical medicine and rehabilitation of the Medical Society of the State of Pennsylvania, has been cited by President Eisenhower "for outstanding service in promoting equal opportunity in employment for the physically handicapped." He also has received the award given annually to one person in each state by the President's Committee on Employment of the Physically Handicapped. Dr. Martucci is associate professor of physical medicine and rehabilitation, University of Pennsylvania Graduate School of Medicine; associate professor of medicine, Woman's Medical College of Pennsylvania; clinical professor of physical medicine and rehabilitation, Temple University School of Medicine; and chief, department of physical medicine and rehabilitation, Philadelphia General, Episcopal, and Abington (Pa.) Memorial hospitals. He is president of the Pennsylvania Academy of Physical Medicine and Rehabilitation; chairman of the Coordinating Committee for the Handicapped, State of Pennsylvania; and a member of the professional and advisory boards of the United Cerebral Palsy of Pennsylvania and United Cerebral Palsy of Philadelphia and Vicinity.

SOUTH DAKOTA

Lectureships in Medical Sciences.—The South Dakota chapter of the Student American Medical Association will sponsor the first of an annual series of lectureships in medical sciences at the University of South Dakota School of Medical Sciences, Vermillion, Nov. 16. The speaker will be Horace W. Magoun, Ph.D., professor of anatomy, University of California at Los Angeles School of Medicine.

GENERAL

Meeting of Arteriosclerosis Society.—The 10th annual meeting of the American Society for the Study of Arteriosclerosis will be held at the Palmer House, Chicago, Nov. 11-12. The presidential address will be delivered Sunday at 2:30 p. m. by Dr. Arthur C. Corcoran, Cleveland. The guest lecturer at the luncheon Sunday, 12 noon, will be Dr. Donald Mainland, professor of medical statistics, New York University College of Medicine, New York, who will present "Safety in Numbers." In all, 69 papers will be presented during the sessions. A reception for the 10 past-presidents and their ladies will be held Sunday, 6:30-7:30 p. m. (dress, semiformal).

Meeting on Research in Psychiatry.—The Regional Research Conference of the American Psychiatric Association will be held in Philadelphia on Nov. 16-17. The program of the meeting is entitled "Research in Psychiatry with Special Reference to Drug Therapy." The academic address entitled "Drugs in Psychiatric Research" will be given by Dr. Abraham Wikler of the U. S. Public Health Service Hospital, Lexington, Ky. Meetings on new drugs in psychiatry and methodology in psychiatric research will be under the chairmanships of Dr. Jay L. Hoffman and Dr. David M. Rioch from Washington, D. C. Presentations of investigations will be made by the investigators individually and then in the form of panel discussions.

Meeting of College of Preventive Medicine.—The third annual meeting of the American College of Preventive Medicine will be held in Atlantic City, N. J., Nov. 14-15, under the presidency of Dr. Charles F. Sutton, Springfield, Ill. The meeting will open at 8 p. m. Wednesday at the Ritz-Carlton Hotel with "Changing Public Apathy to Public Action in the Prevention of Disease: The Social Science Approach" by Dr. Henry Van Zile Hyde, Washington, D. C. The Thursday morning program at Convention Hall will open with "Heart Disease in Relation to Employment" by Dr. Leonard J. Goldwater, New York, followed by "Preventive Medicine Aspects of Ionizing Radiation" by Col. John R. Hall Jr., Medical Corps, U. S. Army, Washington, D. C., and "Chemotherapy in Tuberculosis: Progress and Promise" by Dr. Rufus T. Payne, Augusta, Ga.

Visual Optics Conference.—The bureau of visual science of the American Optical Company will present the third of a series of conferences on visual optics and refraction for ophthalmologists in Southbridge, Mass., Nov. 12-14. The sessions will include a lecture entitled "Correction of Subnormal Vision" by Dr. Gerald Fonda, New York, and "Indirect Ophthalmoscopy" by Dr. Charles L. Schepens of the Massachusetts Eye and Ear Infirmary, Boston. Subjects to be discussed by staff members of the bureau include "Basic Concepts in Ophthalmic Optics," "Objective Refractive Tests," "Physiological Methods of Determining Multifocal Corrections," "Ophthalmic Lens Characteristics," "The H-R-R- Color Vision Test," "Monoplex Eyes and Implants," and "Clinical Aspects of Aniseikonia." Field trips through the American Optical Company lens and frame plants and the new research center, and demonstrations of recent advances in instrumentation have also been planned. Details may be obtained from the Bureau of Visual Science, American Optical Company, Southbridge, Mass.

Opportunity for Research with Nuclear Reactors.—Applications are now open to college and university faculty members for places in the Oak Ridge Research Participation Program for 1957. This program is designed to disseminate technical information to educational institutions by enabling faculty members to spend usually the three summer months in research in Oak Ridge laboratories. The Oak Ridge salary for the participant is equivalent to his university salary. The research participation program is one of the oldest continuous programs of the Oak Ridge Institute of Nuclear Studies, which operates under direct contract with the U. S. Atomic Energy Commission. Applications for three-month summer appointments in 1957 should be returned to the University Relations Division, Oak Ridge Institute of Nuclear Studies, P. O. Box 117, Oak Ridge, Tenn., by Dec. 15, 1956. Information may also be obtained from the University Relations Division.

The medical division of the institute conducts extensive studies of the internal and external uses of radioisotopes in the diagnosis and treatment of cancer and associated diseases, and studies in radiation physics. In the special training division there are opportunities for research in instrumentation, radioisotope applications, and the occurrence of radioactivity in ores and sea water.

Annual Meeting on Cerebral Palsy.—The 10th annual session of the American Academy for Cerebral Palsy will be held at the Congress Hotel, Chicago, Nov. 17-19, under the presidency of Dr. Margaret H. Jones, Los Angeles, who will deliver an address at 3 p. m. Saturday. Instructional courses will be given each day in addition to the formal program. Papers to be delivered during the sessions include:

Chemopallidectomy in Involuntary Movement Disorders, Irving S. Cooper, New York

A Rating Scale for Evaluation of Language Development in the Preschool Cerebral Palsied Child, Michael D'Asaro, Ph.D., Irvin Lehroff, Ph.D., Ida L. Zimmerman, Ph.D., and Margaret H. Jones, Los Angeles.

Ways in Which Physicians Influence the Attitudes of Parents of Cerebral Palsied Children, Eugene T. McDonald, Ed.D., University Park, Pa., and Forrest G. Moyer, Allentown, Pa

Effect of a Superimposed Respiratory Pattern (Electrolung) on the Speech and Breathing of the Athetoid Child, Frank B. Wilson, Ph.D., and Meyer A. Perlstein, Chicago

The Government's Stake in Cerebral Palsy Research, Glidden L. Brooks, New York.

The National Institute of Neurological Disease and Blindness, Pearce Bailey, Bethesda, Md

Collaborative Project on Clinical Pathological Correlation in Cerebral Palsy, George W. Anderson, Bethesda, Md.

Report of Brain Registry Committee, Meyer A. Perlstein, Chicago

Project Cerebral Palsy, Webb E. Haymaker, Bethesda, Md

A symposium on drug therapy Sunday at 10.15 a. m. will include presentation of "Meprobromate in Cerebral Palsy" by Dr. Harriet E. Gillette, Atlanta, Ga., "Flexin in Cerebral Palsy" by Drs Margaret Watkins and Martha H. Hale, Dallas, Texas, and "Effects of Reserpine on the Learning Capacity of Cerebral Palsied and Other Brain-Damaged Children" by Dr William H. Bradford, Phillip N. Hood, Ph.D., and Joseph Siegel, Ph.D., Dallas, Texas "Behavior and Vulnerability of the Blood-Brain Barrier in the Newborn" by Dr. Angel Pentschew, Washington, D. C., will be the first presentation in a symposium on basic research Sunday, 2 p. m. Dr. Leonard T. Kurland, Bethesda, Md., will discuss "Epidemiological Considerations in Cerebral Palsy" and William F. Windle, Ph.D., will present "Report of Conference on Asphyxia Neonatorum, Brain Damage, and Impairment of Learning." A symposium on orthopedic surgery Monday, 8:30 a. m. will include presentation of "Combined Adductor-Gracilis Tenotomy and Selective Obturator Nerve Resection for the Correction of Adduction Deformities of the Hips" by Dr. Sidney Keats, Newark, N. J., "Adductor Myotomies" by Drs. Henry H Banks and William T. Green, Boston, and "Supracondylar Wedge Asteotomies" by Dr. Frederick G. Day, Edmonton, Alberta, Canada. The buffet supper will be served in the Gold Room, Saturday, 7 p. m.

LATIN AMERICA

Society News.—New officers of the Sociedad de Patologia Clinica y Laboratorio de Guadalajara include Dr. Salvador Urzua, president; Dr. Porfirio Villegas L., secretary; and Dr. Javier Preciado Araiza, treasurer.

Pathologists Meeting.—The Mexican Society of Pathologists will hold a slide seminar in English in Mexico City Nov. 17, to which interested American pathologists are cordially invited. The conductor of the seminar will be Dr. Franklin M. Foote of Memorial Center for Cancer and Allied Diseases, New York. Details will be supplied by Dr. Jose Curiel, Artez 205, Mexico, D. F.

CORRECTION

Teaching in Pathology at University of Chicago.—In the studies of the curriculum in the basic sciences, published in The Journal, Aug. 25, 1956, the information given concerning the hours of pathology taught at the University of Chicago School of Medicine was incorrect. The correct figures are as follows:

Pathology 301: Lectures or discussions including examinations	31 hours
Laboratory	58 hours
	89 hours
Pathology 302: Lectures or discussions, including examinations	38 hours
Laboratory	55 hours
	93 hours
Total	182 hours

The Journal listed 108 hours. Whereas in most of the medical schools special pathology is given in the sophomore year, the University of Chicago gives such training in the junior year, divided over the year. This represents an additional 63 hours of required pathology. Added to this is surgical pathology, also required in the junior year, with 80 hours, and obstetric and gynecologic pathology, an additional 15 hours.

EXAMINATIONS AND LICENSURE

American Board of Anesthesiology. *Part I.* Various locations, July 19 Final date for filing application is Jan. 19 Sec, Dr. Curtiss B Hickcox, 80 Seymour St., Hartford 15, Conn.

American Board of Internal Medicine Subspecialties *Cardiovascular Disease.* Chicago, Nov. 30 Final date for filing application was June 1 *Gastroenterology* Philadelphia, April 5-6. Final date for filing application is March 1.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time Sec, Dr. Leonard T. Furlow, Washington University School of Medicine St Louis 10

American Board of Obstetrics and Gynecology. *Part I* Various cities of the United States, Canada, and military centers outside the Continental United States, Feb. 1. Candidates must submit case reports to the office of the Secretary within thirty days of being notified of their eligibility to Part I. The cases must be prepared in the manner described in the Bulletin of the board with a duplicate index list. *Part II* Chicago, May 16-25 Request for reexamination in Part II must be received prior to Feb. 1. Sec., Dr. Robert L Faulkner, 2105 Adelbert Road, Cleveland 6, Ohio.

American Board of Ophthalmology. *Oral* St. Louis, Oct. 20-24 *Written* Jan. 21. Final date for filing application was July 1 *Oral* New York, May 23-27, Chicago, Oct. 7-11. Sec, Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland 9, Maine.

American Board of Orthopaedic Surgery. *Oral Part II.* Chicago, January 1957. Final date for filing application was Aug. 15 Sec., Dr. Sam W. Banks, 116 South Michigan Ave, Chicago 3.

American Board of Pediatrics *Oral Part II* New York City, Oct 12-14, and San Francisco, Dec. 7-9. Sec, Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa

American Board of Physical Medicine and Rehabilitation *Parts I and II* New York City, June 8-9. Final date for filing application is March 1, Sec, Dr. Earl C. Elkins, 200 First St., S W., Rochester, Minn

American Board of Plastic Surgery. Miami, Oct. 17-19 Corres Sec, Mrs. Estelle E Hillerich, 4647 Pershing Ave., St Louis 8

American Board of Preventive Medicine *Oral and Written Public Health* Philadelphia, Nov. 8-10. Sec, Dr. Ernest L Stebbins, 615 N Wolfe St, Baltimore, Md

American Board of Psychiatry and Neurology. *Oral* New York, Dec. 10-11 and New Orleans, Mar 18-19. Final date for filing application is Sept. 10. Sec, Dr. David A. Boyd, Jr., 102-110 Second Ave, S W, Rochester, Minn

American Board of Radiology, Tampa, April 1-6. Final date for filing application is Jan 1. Washington, Sept 23-28. Final date for filing application was June 1. Sec., Dr. B. R Kirklin, Kahler Hotel Bldg, Rochester, Minn

American Board of Surgery. *Part I* Various centers throughout the United States and in certain military centers abroad, Oct 31. *Part II* Rochester, Minn., Oct. 15-16, New Haven, Nov. 19-20, Kansas City, Kan., Dec. 10-11; Los Angeles, Jan. 14-15, San Francisco, Jan 17-18, Houston, Feb. 18-19, Nashville, Mar. 11-12, Boston, April 8-9, and New York, June 10-11.

American Board of Urology. February 1957. Sec, Dr. William Niles Wishard, 1711 N. Capital Ave, Indianapolis 7.

Board of Thoracic Surgery. *Written,* Various centers throughout the country, February 1957, and the closing date for registration is Dec. 1, 1956 Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2

GOVERNMENT SERVICES

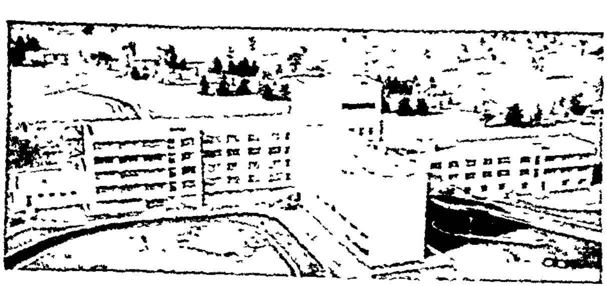
ATOMIC ENERGY COMMISSION

Fellowships in Health Physics Available.—The U. S. Atomic Energy Commission has made available 75 special fellowships for the academic year 1957-1958 in a relatively new field closely related to the atomic-energy program—radiological physics. The Oak Ridge Institute of Nuclear Studies administers the fellowships for the commission. Radiological physics, or health physics, is devoted to the prevention of damage to life or property from radiation and includes such considerations as the disposal of radioactive wastes, biological effects of radiation, the establishment of maximum permissible radiation doses, and the interaction of radiation with matter. The radiological physics program provides for an academic year of formal courses at one of four universities to which fellows may be assigned, followed by a transfer to a corresponding cooperating AEC installation, where fellows train for about three months in applied health physics. The four centers of the program are at the University of Rochester, in cooperation with Brookhaven National Laboratory; the University of Kansas and the University of Washington, in cooperation with the Handord Works; and Vanderbilt University, in cooperation with Oak Ridge National Laboratory. The programs at all four centers will include training in modern physics, radiation biology, radiation instrumentation, industrial hygiene and toxicology, biology, and research.

The basic stipend for AEC fellows is $2,500, with an additional $350 allowed for the spouse and $350 for each dependent child. Fellowship awards include payment of normal tuition and fees required by the university and a travel allowance for the fellow (not for his dependents) from the place of application to his assigned university. Applicants may designate their choice of institutions, although the Oak Ridge Institute of Nuclear Studies cannot guarantee compliance with the choice. Requirements include a bachelor's degree in physics, chemistry, or engineering, acceptability for graduate work at the university, and U. S. citizenship; applicants must be under 35 years of age. Radiological physics fellows should have minors in mathematics, biophysics, or similar fields, although applicants with other qualifications may be considered in special circumstances. Information may be obtained from the Fellowship Office, University Relations Division, Oak Ridge Institute of Nuclear Studies, P. O. Box 117, Oak Ridge, Tenn. Completed applications, supporting letters of reference, and transcripts must reach the institute not later than Feb. 15, 1957, to ensure consideration.

AIR FORCE

New Air Force Hospital at Dayton.—The Air Force dedicated its new 304-bed hospital at the Wright-Patterson Air Force Base in Dayton, Ohio, on Sept. 21. Many physicians and surgeons from throughout the country attended the ceremonies at which the principal speaker was Major Gen. Dan C. Ogle, surgeon general of the Air Force. About 1,000 guests attended. The new hospital cost 6 million dollars and the equipment an additional 1 million dollars. Although rated as a general hospital, it has services not usually found outside specialized institutions. Some of its features are a neuropsychiatric unit, a service for the blind, cold injury treatments, and an arthritis service. It is also the histopathology center for a 19-state area, and it is one of three hospitals in the United States that have a consultation service in aviation medicine. General Ogle pointed out that the Air Force operates more than 200 hospitals throughout the world, 40 of which are 100-bed hospitals or larger, the largest having about 1,000 beds. The Air Force, up to the beginning of this fiscal year, General Ogle said, had obtained approval for the construction of 43 new hospitals within continental United States, 15 of which have been completed and 17 of which are under construction. During this period, it was said, approval had been obtained for the construction of 43 dispensaries, 66 dental clinics, and 10 other miscellaneous medical facilities. A proportionate amount of new construction. General Ogle said, is being accomplished overseas.



New Air Force Hospital, Wright-Patterson Air Force Base, Dayton, Ohio.

ARMY

New Medical Record System.—The new Army health record system becomes effective Jan. 1, 1957; at that time, new regulations on outpatient medical records for nonmilitary personnel also go into effect. Revisions have been made in basic regulations governing individual medical records, clinical records, outpatient medical records, and other recorded data. The outpatient report, one of the three fundamental medical statistical reports, was completely revised as of June, 1956 and new provisions on the morbidity report and the bed and patient reports are now being published. Among other changes now under way are those for the medical follow-up card, the admission and disposition report, and clinical statistics and medical audits.

Under the new system, the Army health record is designed to be a comprehensive medical history of each individual on active duty. It is to be handled so as to be constantly available to medical service personnel, except in periods of actual combat. The different reports will be contained in a folder that accompanies the soldier as a companion to his service record whenever he changes station. While he is on station duty, the folder is in the custody of the medical treatment facility to which he reports for primary medical care. Among other advantages, the new system will minimize the repetition of diagnostic procedures, and might in some instances provide the gain in time needed to save a life. It will reduce correspondence, some of which might be in foreign countries, to obtain information about previous treatment of the soldier. This new record originates when the individual enters the service and has his first physical examination given, his previous medical history outlined, and initial immunization administered. Complete records of all subsequent care are filed in the health folder. Even reports of treatment the individual may receive from civilian or foreign military medical personnel while on active duty are added so the physician treating him may know the whole story.

To provide intensive orientation and to review many details incident to the inauguration of this health record system, the registrars and medical record personnel from Army hospitals throughout the United States and from Europe, Japan, and Puerto Rico assembled at the Walter Reed Medical Center in Washington, D. C., Oct. 8 for a one-week institute conducted by the medical statistics division of the surgeon general's office, where Army and civilian authorities discussed hospital registrar activities and the many changes in the Army's new system of medical records and reports.

Dependents' Medical Care Program.—The surgeon general announces that Major Gen. Paul I. Robinson has been appointed executive director of the new dependents' civilian medical care program. He will head a program to implement a bill enacted by Congress on June 7 providing for medical care in civilian facilities to dependents of active duty military personnel of the "uniformed services." The Army has been designated the executive agent for the "medicare" program. Major General Robinson will be particularly concerned with the arrangement for medical care received from civilian sources for the wives and children of those in the Army, Navy, Air Force, Public Health Service, Coast and Geodetic Survey, and Coast Guard. About 800,000 persons in this category have not received medical care previously because they have not resided near military medical facilities.

NAVY

Transfer to Regular Navy.—The following Naval Reserve medical officers have recently been commissioned in the Medical Corps of the regular Navy: lieutenants R. W. Frazier, E. D. Kaufmann, T. A. Daane, D. L. McCord, David C. Owen, A. K. Rhodes, D. L. Seig, R. I. Sorenson, R. W. Taylor and C. C. Welch.

VETERANS ADMINISTRATION

New Audiology and Speech Correction Chief.—Bernard M. Anderman, Ed.D., chief audiologist of the VA regional office in New York City, has been appointed chief of audiology and speech correction in the VA department of medicine and surgery, Washington, D. C. Dr. Anderman will devote much of his time to the VA program for the reassessment of hearing impairment. Other duties will include programs for hearing aid selection, auditory rehabilitation, and research in audition. He is a member of the American Speech and Hearing Association and formerly was vice-president of the Audiology Study Group of New York City.

Review of Compensation and Pension Claims.—Two years ago the Veterans Administration began a comprehensive review of compensation and pension claims in order to recheck the accuracy of payments made shortly after World War II, when the VA was receiving hundreds of thousands of claims a month and had to train new employees to handle the applications. Eventually, the review will cover 1,713,000 cases of World War II or peacetime veterans under 55 years of age who are receiving compensation for service-connected disabilities. The review is expected to be completed in three or four years. To date, 572,800 such claims have undergone review. In its progress report released Sept. 27, the VA stated that adjustments were found necessary in 30,173 cases or 5.3% of the total claims reviewed thus far.

Following is a comparative breakdown of the adjustments made by the VA:

	Dec 31, 1955	March 31, 1956	June 30, 1956
Increases in monthly payments	2,230	3,263	3,885
Decreases in monthly payments	8,580	10,998	13,290
Terminations of payments	7,989	10,494	12,998
Total	18,799	24,755	30,173

The increases or decreases were made primarily to match the current degree of disability. Of the 12,998 terminations, 10,456 were ended primarily because of improvement in the condition of the patient to such a level that monetary awards are no longer justified, and 2,512 were terminated through severance of service-connection after the VA found "clear and unmistakable error" in associating the disability with the period of service.

The VA said that the 10,456 veterans in the first category have confirmed service-connected disabilities and may be returned to the compensation rolls if those ailments again become disabling.

PUBLIC HEALTH SERVICE

Psychopharmacology Service Center.—The Public Health Service has established a new unit to assist in the development of scientifically sound research programs on tranquilizing and other drugs used in the treatment of mental illness, Surgeon General Leroy E. Burney announced Oct. 16. The new unit is called the Psychopharmacology Service Center in the National Institute of Mental Health in Bethesda, Md. Congress this year appropriated 2 million dollars for an intensive research program to study these drugs. Under the auspices of the National Intitute of Mental Health, the center will be responsible for developing a nationwide research program to stimulate support for basic research and preclinical and early screening and testing of tranquilizing and similar drugs. Dr. Jonathan O. Cole has been appointed psychiatrist in charge of the center. As activities of the center develop, Dr. Burney said, technical assistance and research advisory services will be provided to scientists.

Expanding the Commissioned Reserve.—The U. S. Public Health Service has announced the appointment of 117 physicians, nurses, dentists, sanitary engineers, veterinarians, scientists, therapists, and pharmacists to the inactive reserve of its commissioned officer corps. The service is expanding its inactive reserve by organizing and training medical and health personnel throughout the United States and its territories for duty in times of national emergency. Such emergencies might involve the devastation of cities, extensive illness and death from man-made or naturally occurring disease outbreaks, or the disruption of community life caused by hurricanes, floods, earthquakes, and other natural disasters. These officers will serve in the capacities for which their professional training and experience have fitted them. They will be called out principally to reinforce the staffs of official state and local health agencies and to augment the Public Health Service operating staff.

Studies on Air Pollution.—The Public Health Service has allocated $468,025 to other federal agencies for research in community air-pollution work. The Weather Bureau, Department of Commerce, will continue studies started last year on the dispersal of contaminants in the atmosphere. The National Bureau of Standards will undertake to develop rapid field methods of analysis to determine individual substances in the atmosphere. The U. S. Bureau of Mines will continue its investigation of the causes of inadequate incineration of combustible wastes and the means of improving incineration.

Last year the Library of Congress began to prepare a continuing annotated bibliography on air pollution, including references to the physical, biological, engineering, legal-administrative, and economic aspects of atmospheric pollution. To continue this work during the current fiscal year, the Public Health Service has allocated $17,525 to the library. The Department of Agriculture will assign personnel to the Public Health Service to conduct studies of plants as air-pollution indicators. In addition to the agreements noted above, the surgeon general has announced the award of 12 grants, totaling $318,568, for air-pollution research by nonfederal institutions. Various air-pollution studies are also being conducted within the service's own facilities and through contracts with nongovernmental research groups.

Examination for Microbiologists.—Scientists in the field of microbiology may now take examinations for civil service employment with the U. S. Public Health Service's Communicable Disease Center in Atlanta, Ga., or at center activities throughout the country. This category includes bacteriologists, immunoserologists, mycologists, parasitologists, and virologists. Starting salaries range from $5,440 to $11,610, depending on experience and training and the position to be filled. No written test is required. The Communicable Disease Center is the branch of the Public Health Service that plans, coordinates, and provides assistance to state and local health agencies in the control of communicable diseases.

Scientists in the medical microbiologist positions are concerned with research and developmental and investigative work in the specialized fields of pathogenic micro-organisms. Scientists in the higher grades provide scientific and administrative direction in research programs in the specialized fields, determine projects to be initiated, consult with outside authorities, and conduct important research in the specialized field. Information may be obtained from any post office except in civil service regional headquarters cities, or from the U. S. Civil Service Examiners, Communicable Disease Center, Atlanta, Ga.

FOOD AND DRUG ADMINISTRATION

Joint Study of Adverse Drug Reactions.—Prompt reporting of unusual or adverse reactions to drugs is the objective of a new joint study being carried on by 11 leading hospitals, the Food and Drug Administration announced Oct. 17. The pilot reporting system, sponsored by the administration, has been undertaken to obtain information regarding effects that may appear in some patients when drugs are administered to large numbers of people. This problem has been magnified by the increasing number of potent new drugs. Even the most extensive clinical studies cannot forecast all types of drug reactions that may develop throughout the population. The administration said that hospitals provide an ideal site for observing the effects of drugs and obtaining essential information that is not available from other sources. This joint study is being undertaken in the interest of public health, better patient care, and the safe use of drugs.

DEATHS

Weidman, Frederick De Forest, Philadelphia; born in Bristol, Conn., Oct. 16, 1881; University of Pennsylvania Department of Medicine, Philadelphia, 1908; emeritus professor of research in dermatology and mycology at his alma mater, where he served as assistant demonstrator in pathology and normal histology, instructor in gross morbid anatomy, assistant director of the laboratory of dermatological research, acting head of the department of dermatology and syphilology, and in 1923 became professor of dermatological research; for many years on the faculty of the University of Pennsylvania Graduate School of Medicine, where in 1953 he became emeritus professor of research in dermatology and mycology; professor of pathology at the Woman's Medical College of Pennsylvania from 1914 to 1917; specialist certified by the American Board of Dermatology and Syphilology, of which he was vice-president and for many years a member; past-president and secretary of the American Dermatological Association; past-president of the American Academy of Dermatology and Syphilology, Philadelphia Pathological Society, and the Society for Investigative Dermatology; and associate member of the American Medical Association; member of numerous foreign dermatological societies; assistant and later associate pathologist, Philadelphia Zoological Gardens, from 1910 to 1954; served on the staffs of the Philadelphia General Hospital and the Graduate Hospital of the University of Pennsylvania; from 1946 to 1954 consultant, U. S. Naval Hospital and Valley Forge (Pa.) Hospital; during World War II was consultant in tropical medicine to the Secretary of War; served as associate editor of the *Archives of Dermatology and Syphilology*, and of *Mycopathologia et Mycologia Applicata;* a collaborator in Davis' "Cyclopedia of Medicine" and in Appleton's "Practitioner's Library of Medicine and Surgery"; on the editorial board of the *Journal of Investigative Dermatology*, which dedicated its *Festschrift* number to him in the March, 1952, issue; the Nov. 18, 1950, issue of *Modern Medicine* had a symposium on dermatology dedicated to him; died while vacationing at Bailey Island, Maine, Aug. 30, aged 74, of coronary thrombosis.

Siegel, William ⊕ Albany, N. Y.; born Aug. 9, 1895; University and Bellevue Hospital Medical College, New York City, 1918; specialist certified by the American Board of Preventive Medicine; member of the American Trudeau Society and the American Public Health Association; joined the state health department in 1927 as a clinical physician and in 1930 was promoted to associate director of the division of tuberculosis; in July, 1935, was made director of the division and in 1946, director of the tuberculosis case find bureau; after retirement in April, 1955, remained as consultant in the department's division of tuberculosis control; past vice-president of the State Civil Service Employees Association; resident physician from 1919 to 1922 at the Maryland Tuberculosis Sanatorium in State Sanatorium; died Aug. 30, aged 61, of metastatic melanoma.

Cerniglia, Frank Joseph ⊕ Elmhurst, N. Y.; Long Island College Hospital, Brooklyn, 1928; assistant clinical professor of surgery at the New York Homeopathic Medical College and Flower Hospital, New York City; fellow of the American College of Surgeons and the International College of Surgeons; past-president of the Medical Society of the County of Queens, of which he was a trustee, and the Queensboro Surgical Society; member of the planning committee of the Queensboro Council for Social Welfare and member of the council of the Queensboro Tuberculosis and Health Association; on the staffs of the Queens General Hospital, Creedmoor State Hospital, and the Jamaica Hospital in Jamaica; died Sept. 2, aged 52, of heart disease.

Kerr, LeGrand, Sayville, N. Y.; born in New York City in 1870; Bellevue Hospital Medical College, New York City, 1892; an associate member of the American Medical Association; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; a founder of the Brooklyn Academy of Pediatrics; served as president of the Medical Association of Greater New York; fellow of the American College of Physicians, of which he was a counselor; on the staffs of the Methodist and Swedish hospitals in Brooklyn, Nassau Hospital in Mineola, and the Rockaway Beach (N. Y.) Hospital; died Aug. 10, aged 85, of cerebral hemorrhage.

Albertson, Horace Allen ⊕ Roanoke, Va.; born in Richmond May 25, 1918; Medical College of Virginia, Richmond, 1943; also a graduate in pharmacy; interned at Johns Hopkins Hospital in Baltimore; formerly a resident at the Jefferson Hospital in Roanoke, where he was later on the staff; served a residency at the Veterans Administration Hospital in Newington, Conn.; specialist certified by the American Board of Surgery; member of the Southeastern Surgical Congress; fellow of the American College of Surgeons; at one time clinical instructor in surgery at Yale University School of Medicine in New Haven, Conn.; veteran of World War II; died Aug. 20, aged 38.

LeBreton, Prescott, St. Petersburg, Fla.; born in Paterson, N. J., Nov. 4, 1872; Columbia University College of Physicians and Surgeons, New York City, 1896; an associate member of the American Medical Association; specialist certified by the American Board of Orthopaedic Surgery; member of the American Orthopaedic Association and the American Academy of Orthopaedic Surgeons; fellow of the American College of Surgeons; on the staffs of the American Legion Hospital for Crippled Children, St. Anthony's Hospital, and the Mound Park Hospital; died in Middletown, N. Y., July 26, aged 83.

Aiken, Marshall Herbert ⊕ Tiffin, Ohio; Western Reserve University School of Medicine, Cleveland, 1934; died Aug. 3, aged 48.

Anderson, William Laurence, DeBary, Fla.; Tufts College Medical School, Boston, 1914; for many years on the board of education of Staten Island, N. Y.; died in Burlington, Vt., Aug. 10, aged 73, of coronary sclerosis.

Avison, Oliver R., St. Petersburg, Fla.; Victoria University Medical Department, Coburg, Ontario, Canada, 1887; a Presbyterian medical missionary in Korea for many years; first president of the Chosen (Korea) Christian College; died Aug. 28, aged 96, of arteriosclerotic heart disease.

Balofsky, Samuel Lawrence ⊕ Detroit; Tulane University School of Medicine, New Orleans, 1932; associate professor of radiology at Wayne University College of Medicine; specialist certified by the American Board of Radiology; on the staffs of the Detroit Memorial Hospital and the City of Detroit Receiving Hospital, where he died Aug. 11, aged 47.

Bendshadler, George Henry, Portland, Ore.; University of Oregon Medical School, Portland, 1924; certified by the National Board of Medical Examiners; member of the American Academy of General Practice; veteran of World War I; died in the Emanuel Hospital Aug. 22, aged 67, of ruptured aorta.

Booker, Lyle Steele ⊕ Waynesboro, Va.; University College of Medicine, Richmond, 1908; instrumental in the founding of the Waynesboro Community Hospital, where he died Aug. 10, aged 72, of arteriosclerosis.

Burke, John Henry, Elmira, N. Y.; University of Buffalo School of Medicine, Buffalo, 1904; an associate member of the American Medical Association; consultant on the staff of St. Joseph's Hospital, where he died Aug. 19, aged 73, of arteriosclerotic heart disease.

Burns, Frederick John, Otisville, Mich., the Hahnemann Medical College and Hospital, Chicago, 1906; died in Flint Aug. 12, aged 80, of cerebral vascular accident.

Bush, William Bert, St. Louis; Barnes Medical College, St. Louis, 1911; also a dentist; died Aug. 17, aged 79.

Cahoon, Grace Wilson, Los Angeles; University of Minnesota College of Medicine and Surgery, Minneapolis, 1897; at one time practiced in Butte, Mont., and was secretary of the Bow County Medical Society; died July 22, aged 84, of coronary thrombosis.

Carlton, Charles E. ⊕ Stoutland, Mo.; Kansas City (Mo.) Medical College, 1901; on the staff of the Louise G. Wallace Hospital in Lebanon; died Aug. 2, aged 79, of cerebral hemorrhage.

⊕ Indicates Member of the American Medical Association.

Conaway, Benjamin Franklin, Mannington, W. Va.; Maryland Medical College, Baltimore, 1908; died Aug. 28, aged 78, of arteriosclerotic heart disease.

Copp, Francis Allen ⊕ *Jacksonville, Fla.*; Tulane University School of Medicine, New Orleans, 1918; veteran of World War I; died Aug. 7, aged 62.

Corper, Franklin Joseph ⊕ *Skokie, Ill.*; Northwestern University Medical School, Chicago, 1917; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; on the staff of the Evanston (Ill.) Hospital, where he died Aug. 25, aged 64, of carcinoma of the head of the pancreas.

Crumb, Jaynes Mott, South Otselic, N. Y.; University of Vermont College of Medicine, Burlington, 1902; an associate fellow of the American Medical Association; died in Binghamton Aug. 29, aged 78, of pneumonia.

Daves, Vergil C. ⊕ Vienna, Ga.; Atlanta School of Medicine, Atlanta, 1913; served as state senator and as county physician; on the staff of the Dooly Hospital; died in Macon July 12, aged 69, of coronary thrombosis.

Folkman, Nathan ⊕ Brooklyn, N. Y.; Hahnemann Medical College and Hospital of Philadelphia, 1930; president-elect of the Kings County Surgical Society; veteran of World War II; taught anatomy at Long Island College of Medicine; on the staffs of the Cumberland, Prospect Heights, and Swedish hospitals; died in Lenox, Mass., Aug. 8, aged 48, of coronary thrombosis.

Frank, George Washington, Des Moines, Iowa; State University of Iowa College of Medicine, Iowa City, 1898; veteran of World War I; member of Veterans of Foreign Wars; for many years on the staff of the Veteran Administration Hospital, where he died July 30, aged 80, of coronary occlusion.

Gregg, William T. S. ⊕ Cambridge, Mass.; Michigan College of Medicine and Surgery, Detroit, 1892; member of the Michigan State Medical Society and the American Roentgen Ray Society; formerly on the staff of the Calumet and Hecla Hospital in Calumet, Mich.; formerly health officer in Calumet; died July 15, aged 85, of coronary thrombosis.

Hewes, Ara Bird ⊕ Adrian, Mich.; Cleveland Homeopathic Medical College, Cleveland, 1903; past-president and for a term secretary-treasurer of the Lenawee County Medical Society; veteran of the Spanish-American War and World War I; on the staff of the Emma L. Bixby Hospital; died July 30, aged 82, of coronary thrombosis.

Holzberg, Henry Leopold, San Francisco; University of California School of Medicine, San Francisco, 1915; veteran of World War I; died Aug. 6, aged 63, of carcinoma of the thyroid.

Huycke, Austin H. ⊕ Oregon City, Ore.; McGill University Faculty of Medicine, Montreal, Quebec, Canada, 1907; died in St. Vincent's Hospital, Portland, July 17, aged 74.

Hyman, Abraham Harry, Faust, N. Y.; University and Bellevue Hospital Medical College, New York City, 1910; member of the staff of the Mercy General Hospital in Tupper Lake, where he died July 30, aged 72, of heart disease.

Kamman, George Henry ⊕ Seymour, Ind.; Kentucky School of Medicine, Louisville, 1900; for many years city health officer; secretary of the board of health; on the staff of the Jackson County Schneck Memorial Hospital; died July 20, aged 86, of coronary occlusion.

Kendall, Clarence Fairbanks ⊕ Biddeford, Maine; Medical School of Maine, Portland, 1901; veteran of World War I; served as state district health officer, commissioner of health for the state health department, and with the U. S. Public Health Service; died Aug. 22, aged 80.

King, Hamilton Theodore, Newport, R. I.; Harvard Medical School, Boston, 1904; veteran of World War I; formerly practiced in Joliet, Ill., where he was on the staffs of the Silver Cross and St. Joseph's hospitals; died July 19, aged 76, of pyelonephritis.

Kirkman, Leroy Gresham ⊕ Springfield, N. J.; Columbia University College of Physicians and Surgeons, New York City, 1900; for many years practiced in Newark, where he was on the staffs of St. Michael's Hospital and the Presbyterian Hospital, where he died Aug. 3, aged 80, of coronary thrombosis.

Kohn, Louis Winfield ⊕ New York City; University of Maryland School of Medicine, Baltimore, 1910; specialist certified by the American Board of Internal Medicine; member of the American College of Gastroenterology and the Endocrine Society; fellow of the American College of Physicians; died Aug. 16, aged 67, of a heart attack.

Kolb, Isaac Newton ⊕ Blanchard, Okla.; St. Louis College of Physicians and Surgeons, St. Louis, 1923; died July 31, aged 74, of coronary heart disease.

Livingstone, Joseph William ⊕ Hudson, Wis.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, Chicago, 1905; past-president of the St. Croix Pierce Counties Medical Society; veteran of World War I; served as health officer; died in St. John's Hospital, St. Paul, Minn., July 25, aged 75, of pulmonary emphysema.

McGavin, Agnes Purcell, Morristown, N. J.; University of Toronto Faculty of Medicine, Toronto, Ontario, Canada, 1920; member of the American Psychiatric Association; director of the mental hygiene clinic at the New Jersey State Hospital at Greystone Park; died in the Morristown Memorial Hospital May 6, aged 62, of cancer.

Markowitz, Benjamin ⊕ Bloomington, Ill.; Loyola University School of Medicine, Chicago, 1922; specialist certified by the American Board of Pathology; fellow of the American College of Physicians; member of the College of American Pathologists and the American Society of Clinical Pathologists; past-president of the Illinois Society of Pathologists; served as health officer of Bloomington; pathologist, Brokaw Hospital in Normal, St. Joseph's and Mennonite hospitals; died Sept. 17, aged 60, of prostatic cancer with metastases.

Mast, Earl Cletus ⊕ Mansfield, Ohio; Columbia University College of Physicians and Surgeons, New York City, 1937; member of the American Society of Anesthesiologists; on the staff of the Mansfield General Hospital; died Aug. 19, aged 51, of coronary thrombosis.

Morgans, Dollie Earle, Nashville, Tenn.; Medizinische Fakultät der Universität, Vienna, Austria, 1933; interned at the Henrotin Hospital in Chicago, where she served a residency; formerly a resident at the Illinois Masonic Hospital in Chicago and the Veterans Administration Hospital in Little Rock, Ark.; during World War II served as a second lieutenant in the WAC; died in Miami, Fla., Aug. 8, aged 49.

Murphy, Michael Joseph, Brooklyn, N. Y.; Tufts College Medical School, Boston, 1926; fellow of the American College of Surgeons; veteran of World War II; member of the Medical Society of the State of New York; on the staffs of the St. Mary's, St. Peter's, and the Kings County hospitals; died Aug. 31, aged 58, of coronary disease.

Nichols, Elijah Emera, Pikesville, Md.; University of Maryland School of Medicine, Baltimore, 1911; an associate member of the American Medical Association; died April 6, aged 70, of hypertensive arteriosclerotic heart disease.

Owens, Russell Wayne, Salt Lake City; University of Pennsylvania School of Medicine, Philadelphia, 1920; member of the Utah State Medical Association and the American Academy of General Practice; veteran of World War I; member of the senior staff, Dr. W. H. Groves Latter-Day Saints Hospital; died Aug. 27, aged 60, of chronic cor pulmonale.

Patterson, Frank ⊕ Tyrone, Pa.; Baltimore Medical College, Baltimore, 1902; formerly medical examiner for the Pennsylvania Railroad in Altoona; served on the staff of the Hollidaysburg (Pa.) State Hospital; member of the American Psychiatric Association; died in the Tyrone hospital July 19, aged 78.

Perkins, Edgar Verne ⊕ Chicago; Chicago College of Medicine and Surgery, Chicago, 1913; on the staff of the Evangelical Hospital, where he died Aug. 28, aged 69, of ruptured peptic ulcer.

Poulton, James Elmer ⊕ Staten Island, N. Y.; Northwestern University Medical School, Chicago, 1936; served as secretary of the Richmond County Medical Society; on the staff of the Staten Island Hospital; separated from the U. S. Public Health Service Jan. 10, 1938; died while on vacation at Lake Louise, Alberta, Canada, Aug. 31, aged 50, of coronary thrombosis.

Punche, Albert Emerson, Detroit; University of Illinois College of Medicine, Chicago, 1914; died in the Veterans Administration Hospital, Dearborn, July 2, aged 81, of intestinal obstruction, cancer of the colon, and cerebral arteriosclerosis.

Reed, F. Grendon, Whallonsburg, N. Y.; New York Homeopathic Medical College and Flower Hospital, New York City, 1915; died in the Hudson River State Hospital, Poughkeepsie, May 3, aged 68, of chronic (Huntington's) chorea, bronchopneumonia, and arteriosclerotic heart disease.

Regar, Daniel S., Akron, Pa.; Medico-Chirurgical College of Philadelphia, 1904; also a graduate in pharmacy; for many years member of the board of health; died July 17, aged 87.

Rhea, Clarance Ward, West Allis, Wis.; St. Louis University School of Medicine, St. Louis, 1918; veteran of World War II; served in the regional office of the Veterans Administration in Kansas City, Mo.; at one time on the staff of the Veterans Administration Hospital in Wood; died Aug. 24, aged 65.

Ross, Samuel Tulloch ⊕ Nashville, Tenn.; Vanderbilt University School of Medicine, Nashville, 1915; fellow of the American College of Surgeons; on the staff of the Nashville General Hospital; died in the Mid-State Baptist Hospital July 23, aged 66, of cerebral hemorrhage.

Schoor, William Frederick ⊕ Hutchinson, Kan.; University Medical College of Kansas City, Mo., 1904; served as county coroner; on the staff of the Grace Hospital, where he died June 22, aged 79.

Sohmer, Alphonse Edward John ⊕ Mankato, Minn.; Long Island College Hospital, Brooklyn, N. Y., 1899; fellow of the American College of Surgeons; past-president of the Southern Minnesota Medical Association; past vice-president of the Minnesota State Medical Association; on the staffs of the Immanuel and St. Joseph's hospitals; died Sept. 4, aged 77.

Steffens, Georgia Wetmore, Evanston, Ill.; the Hahnemann Medical College and Hospital, Chicago, 1918; died in Batavia Sept. 10, aged 73, of cerebral arteriosclerosis.

Stephens, James B., Oxford, Miss. (licensed in Tennessee in 1913); member of the Mississippi State Medical Association; died in Water Valley April 24, aged 68, of status asthmaticus.

Steward, W. Benjamin ⊕ Millbrae, Calif.; University Medical College of Kansas City, Mo., 1908; formerly practiced in Topeka, Kan., where he was on the medical and surgical staff of St. Francis Hospital; served on the staffs of the Hollywood Presbyterian Hospital in Los Angeles and the Physicians and Surgeons Hospital in Glendale, Calif.; died in the Peninsula Hospital Aug. 24, aged 76, of complications following a coronary occlusion suffered last December.

Taylor, Robert Stanley ⊕ Bay City, Mich.; University of Michigan Medical School, Ann Arbor, 1948; veteran of World War II; died in the Mercy Hospital Aug. 2, aged 35, of acute coronary occlusion.

Tedesco, Ignatius, New Orleans; Tulane University of Louisiana School of Medicine, New Orleans, 1913; an associate member of the American Medical Association; on the staff of Hotel Dieu, Sisters' Hospital; died July 24, aged 67, of congestive heart disease.

Thomas, Herbert Alfred ⊕ Lima, Ohio; Western Reserve University Medical Department, Cleveland, 1909; on the staff of the Lima Memorial Hospital; died in the Cleveland (Ohio) Clinic Hospital Aug. 17, aged 76, of cardiac arrest.

Tidyman, Gay F., Joliet, Mont.; Northwestern University Medical School, Chicago, 1900; an associate member of the American Medical Association; veteran of the Spanish-American War; formerly surgeon general of the National Department of the U. S. Spanish-American War Veterans; past-president of the Madison County (Mont.) Medical Society; died in Billings July 10, aged 83, of a heart attack.

Titus, Peter Franklin ⊕ Watertown, Mass.; Middlesex University School of Medicine, Waltham, 1942; interned at the Tampa Municipal Hospital in Tampa, Fla.; formerly a resident at the Doctors Hospital and Bellevue Hospital in New York City; resident physician in the ophthalmology department, George F. Geisinger Memorial Hospital and Foss Clinic in Danville, Pa.; formerly a captain in the U. S. Army Reserve; died July 5, aged 44, of a coronary attack.

Trippett, Lemuel Harrison, Jr. ⊕ Amigo, W. Va.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1918; president of the Wyoming County Medical Society; died Sept. 6, aged 60, of coronary occlusion.

Vandale, Albert Leroy, Pawtucket, R. I.; Tufts College Medical School, Boston, 1926; veteran of World War II; for many years superintendent of health of Pawtucket; on the staffs of the Notre Dame Hospital in Central Falls, Roger Williams General and St. Joseph's hospitals in Providence, and the Memorial Hospital; died July 16, aged 58, of carcinoma of the sigmoid with metastases.

Wallis, Otto ⊕ Chicago; Medizinische Fakultät der Universität, Vienna, Austria, 1926; on the staffs of the Frank Cuneo Memorial Hospital and the Columbus Hospital, where he died Sept. 9, aged 55, of coronary insufficiency.

Washburn, Clayton D. ⊕ Jacksonville, Fla.; University of Pennsylvania Department of Medicine, Philadelphia, 1902; on the staff of St. Luke's Hospital; died July 17, aged 82, of dissecting aortic aneurysm.

Weakley, Bertram M., Indianapolis; Medical College of Ohio, Cincinnati, 1904; died July 15, aged 85.

Wender, Max, New York City; University and Bellevue Hospital Medical College, New York City, 1911; on the staffs of the Mount Sinai and Sydenham hospitals; died Aug. 5, aged 69.

Wick, Hilton Addison, New Bethlehem, Pa.; Jefferson Medical College of Philadelphia, 1917; veteran of World War I; served as school director; died in the Maple Avenue Hospital, Du Bois, June 15, aged 62, of congestive heart disease and lung cancer.

Wolf, Richard S., Rochester, N. Y.; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1919; on the staff of the Rochester State Hospital; died in the Rochester General Hospital Aug. 6, aged 65, of coronary occlusion.

Woodard, Albert G., Goldsboro, N. C.; University of North Carolina School of Medicine, Chapel Hill, 1907; member of the Medical Society of the State of North Carolina; past-president of the North Carolina Eye, Ear, Nose and Throat Society; past-president and secretary of the Wayne County Medical Society; died in the State Hospital in Morganton July 20, aged 74.

Wright, John Marion ⊕ Hernando, Miss.; Kentucky University Medical Department, Louisville, 1905; died in Memphis, Tenn., Aug. 23, aged 73, of coronary thrombosis and arteriosclerosis.

Wyatt, Fred Howard ⊕ Denver; General Medical College, Chicago, 1924; member of the Indiana State Medical Association; died July 14, aged 69, of pulmonary embolism.

Zaiser, Harry Edgar, Fullerton, Calif.; St. Louis College of Physicians and Surgeons, St. Louis, 1902; fellow of the American College of Surgeons; an associate member of the American Medical Association; for 31 years superintendent of the Orange County General Hospital in Orange; died Aug. 1, aged 76.

Zaur, Israel Sidney ⊕ Bridgeport, Conn.; Yale University School of Medicine, New Haven, 1932; certified by the National Board of Medical Examiners; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; veteran of World War II; member of the consulting staff at the Bridgeport Hospital, where he was formerly chief of staff and where he died July 18, aged 48.

Zimmermann, Walter Charles Lee, Oakland, Calif.; Wisconsin College of Physicians and Surgeons, Milwaukee, 1898; died July 25, aged 81, of cardiac failure, cardiovascular renal disease, arteriosclerosis, and hypertension.

Zuber, Thomas Luther, West Point, Miss.; Meharry Medical College, Nashville, Tenn., 1913; veteran of World War I; died July 26, aged 68.

Zuckerman, Jerome John ⊕ New Rochelle, N. Y.; Cornell University Medical College, New York City, 1908; on the courtesy staff of the New Rochelle Hospital, where he died July 21, aged 70.

FOREIGN LETTERS

AUSTRIA

The Reticuloendothelial System.—At the meeting of the Society for Internal Medicine in Vienna on May 17, Dr. H. Fleischhacker stated that the reticuloendothelial system represents a group of cells in various organs that have been considered together because of their common capacity for intravital storage of dyes. It is necessary to differentiate between the phagocytosing reticular cells (which can be demonstrated in the bone marrow, lymph nodes, liver, and spleen and which represent highly developed end-cells) and the plasma cells, which have definite secretory functions. They have been made responsible for the formation of normal plasma albumin and particularly for the elaboration of gamma globulins. In the presence of abnormal conditions, they also produce paraproteins, macroglobulins, Bence Jones' albumin, and amyloid. Because autoantibodies are also globulins, the concept seems to be justified that the plasma cells, particularly in the lymph nodes and spleen, also play a part in the production of antibodies. It may be assumed that the antigenolytic products that are formed by the phagocytosing reticular cells stimulate the new formation of plasma cells, which only then form the antibodies and release them to the circulation (genetic theory). The small and large lymphoid reticular cells are hardly prominent in normal bone marrow specimens but take part in all the stronger reactions and also in the proliferation of reticular and plasma cells.

Cortisone and prednisone prevent the production of autoantibodies by the suppression of the histiocytic function of the reticuloendothelial system, and they definitely inhibit the production of antibodies that may have started already, as shown by the reduction of the antibody titers in the blood. After the giving of cortisone, sensitized erythrocytes, leukocytes, and thrombocytes, which are loaded with antibodies, no longer stimulate phagocytosis. They are subjected only to the normal rate of breaking up, and their duration of life approaches standard values. Furthermore, the effects of the antibody load with its cytolytic influence are stopped in a manner not yet fully explained. Thus may be explained the good results observed in patients with acquired hemolytic anemia, in those with granulocytopenia and agranulocytosis caused by antibodies, and in those with thrombopenia. The inhibitory influence of cortisone on the reticuloendothelial system may be demonstrated also in the presence of proliferations of this cellular system.

Dr. C. Steffen stated that one ascribes to cortisone a specific influence on the defensive powers of the body. The influence on the defense against infection is paralleled by its influence on antibodies. This influence may be exerted on the formation of antibodies, on the breaking up of antibodies in the presence of an increased protein metabolism, on liberated substances of reaction, and on antigen-antibody formation. An influence on liberated substances of reaction is not generally considered. E. Lauda stated that it is not fitting to describe the spleen as the organ of antibody formation. The spleen has nothing to do with the production of antibodies, or at least it has not more to do with it than any other organ that harbors reticular cells. The case of reticulosis in a patient who later on showed a good response to cortisone and whose temperature was restored to normal by the administration of cortisone could also have been presented as one of a febrile infection in which defervescence was obtained with cortisone therapy. Defervescence has nothing to do with reticulosis. Defervescence as a result of cortisone therapy can be seen in every patient with typhoid fever, but this has no relation to reticulosis. The same reaction to cortisone may be observed in any patient with febrile infection, and, although defervescence takes its course with the defense powers of the organism and thus also with the reticuloendothelial system, this type of infection has nothing to do with the old concept of reticulosis.

BRAZIL

Prevention of Leprosy.—At a meeting of leprologists held in São Paulo in July, Dr. Luis Batista stated that the results of the prophylactic measures used in 1924 have not been satisfactory because the incidence of leprosy has increased tremendously. The participants at the meeting recommended a change of policy that includes the following points: 1. Reporting should be compulsory but the identity of the patients should be kept secret. 2. Isolation of the patient need not necessarily be in a hospital. 3. Treatment may be given in clinics or by private physicians. Before such a program can be accepted, the public must be educated regarding the true nature of the disease. It was further recommended that greater emphasis be placed on teaching medical students about leprosy, because early recognition and treatment of the disease is essential to the success of treatment with the sulfones. At present, one of the greatest difficulties of the leprosy service is to find well-trained physicians who are interested in becoming leprologists. Careers in this specialty should be made more attractive.

FRANCE

Pulmonary Tissue Grafts.—P. Ganter and co-workers (*Rev. franç. étud. clin. et biol.* 1:277-295, 1956) made 566 intraocular grafts of pulmonary and other tissues, mainly in mice. Such pulmonary tissue passes through a primary stage of degeneration with cellular alteration and sometimes necrosis, lasting four days. The initial changes resolving completely, the grafted lung tissue, from the fifth day and persisting for 5 to 20 days, shows signs of viability either by maintaining morphological characteristics similar to those of the original tissue or by growth of the graft and the differentiation of certain elements, in particular the bronchial cells. From about the 12th day, two reactions, usually associated, constantly occur in the tissue and eventually result in the complete disruption of the pulmonary tissue. The first is nearly always a conjunctival reaction starting at the center of the graft or at the point of contact of the bronchus and subsequently invading the entire graft. A lymphocytic infiltration that may be so intense as to give the graft the appearance of lymphoid tissue is associated with this reaction. The lymphocytes may be derived from the host and represent a defense reaction against the foreign tissue, but, in some instances at least, the lymphocytes come from the graft itself. The conjunctival reaction, earlier and more intense if the grafted tissue is adult, and in any case in the guinea-pig, results within 20 to 45 days in replacement of the graft by a fibrous scar, which disappears at about the second month and can no longer be identified after three months. The above changes seem independent of the presence or absence of any revascularization of the graft.

The presence of the pulmonary tissue graft is the cause of an inflammatory reaction and changes in the cornea of the host. The most important is a wild proliferation of the anterior corneal epithelium into the graft, with the formation of stratified centers such as are seen in cutaneous epitheliomas. These structures may invade the entire graft, either by direct extension or by embolism along vessels or air ducts, but never extend beyond the graft and are reabsorbed at the same time as the latter, at about two months. This stimulation of a proliferative reaction by the pulmonary tissue is invariably seen when it is in contact with the anterior corneal epithelium. Operative trauma or the presence of a foreign body in the anterior chamber can be excluded as the primary factors in the stimulation of the corneal epithelium. It is possible, however, that they augment this reaction. Pulmonary tissue would appear to be the only one to possess this property of stimulation. The phenomenon has never been observed with other tissues (fat, liver, kidney, skin, intestine, or trachea). It is not essential for pulmonary tissue to maintain an active metabolism to stimulate the proliferative reaction. Pulmonary tissue destroyed by prolonged grinding retains this property,

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The items in these letters are contributed by regular correspondents in the various foreign countries.

although to a lesser degree. It is not proved that bronchial epithelium alone possesses this property, but parenchymal alveolar tissue, with all bronchial tissue removed, certainly does. The proliferative stimulating action of lung tissue is not restricted to corneal epithelium. Cutaneous epithelium, in contact with pulmonary tissue under the same conditions of an intraocular graft, reacts in the same manner, proliferating and forming stratified centers that invade the pulmonary tissue. It would appear that, within certain limits, pulmonary tissue possesses a general stimulating property.

Parietal Fibroplastic Endocarditis. —A. Gerbaux and co-workers at the May 13 meeting of the French Society of Cardiology reported two cases of parietal fibroplastic endocarditis, which brings the cases reported so far to a total of about 20. Clinically the disease has the aspect of a primary global cardiac insufficiency suggestive of Pick's syndrome but with, in addition, a marked eosinophilia. High temperature and renal infection are frequent. The disease is characterized by the presence of a thick fibrous layer covering the parietal endocardium of one or both ventricles. This kind of fibrosis is generally lined with a flattened mural thrombus. In addition there is an endarteritis, or an arrested, dispersed endarteriolitis. There may be lesions suggestive of periarteritis nodosa. According to the authors, the thickening of the endocardium was not due to a simple reaction of the endocardium but to a deposit of fibrin. There is no doubt about the allergic nature of the disease, but its underlying cause remains obscure. In addition to bacterial antigen and a chemical factor, a parasitic origin, particularly filarial, may be the cause in some patients.

Pains After Mitral Commissurotomy.—At the same meeting B. Coblentz and co-workers reported a series of 170 patients on whom mitral commissurotomy had been performed and who had been followed postoperatively for 20 months to five years. In this series 27 patients complained of thoracic or articular pain, occurring during the first weeks after operation. In 15 patients the pain was accompanied by fever, but the late results of the operation were not affected by this complication. The cause of the pain is not known, but a history of rheumatic attacks, focal infection, prolonged operation, or faulty technique are possible factors. On the other hand, it may be a recurrence of an infective endocarditis. Use of aspirin and hormonotherapy seem to be effective and may be of prophylactic value.

Intestinal Cul-de-Sac Following Lateral Anastomosis.—At the meeting of the Society of Surgery in Lille in February, E. Delannoy reported a series of four patients with intestinal cul-de-sacs following lateral ileoileostomy and ileotransversostomy. In some patients this gives rise to symptoms of mild occlusion with relapse. Ulceration on the surface of the stump may give rise to a fistula or peritonitis and in some patients to macrocytic anemia. The authors advise end-to-end anastomosis whenever possible, but, if lateral anastomosis must be done, it should be as near the proximal stump as possible.

Cancer of the Esophagus.—At the same meeting P. Razemon and co-workers reported a series of 41 patients with cancer of the esophagus, 36 of whom were operated on. The maximum survival time was two and one-half years. In spite of the high mortality the authors concluded that an attempt at resection should be made because, if successful, it relieves the patient's progressive dysphagia and alleviates pain.

Cholecystoduodenal Fistula.—Peycelon and P. Replumaz (*Annales de chirurgie Paris*, vol. 32, 1956) say that, in the operative management of cholecystoduodenal fistulas of biliary origin, cholecystectomy may solve the biliary problem unless there are also lesions in the main biliary duct. On the other hand, it may be difficult to suture the duodenal perforation. The authors stress the limited efficiency of duodenorrhaphy and advocate gastroduodenectomy in the treatment of wide duodenal gaps with such duodenal narrowing as makes possible only an approximating or stenosing suture.

Gastric Reticulum Cell Sarcoma.—Rauber and co-workers in the same issue reported a series of five patients with gastric reticulum cell sarcoma. The diagnosis may be suggested by the intensity of the painful syndrome and occasionally by the size of the tumor, which often renders it easily palpable. Roentgenograms may reveal an extramucosal origin of the tumor. On operation, the gross appearance of the tumor may be atypical, and only through histological study is it possible to make the diagnosis. This too may be difficult, particularly in the case of atypical epitheliomas that simulate reticulum cell sarcoma. In most patients gastric reticulum cell sarcoma is rapidly fatal. The only treatment is wide resection. Postoperative roentgenotherapy is only a relatively effective adjuvant.

Meniscal Lesions of the Knee.—Gandin and co-workers in the same issue stated that opaque arthrography is a simple and reliable method for studying the meniscal changes in the knee that frequently occur in sports and military training. It is a valuable aid to the medicolegal assessment of injuries incurred at work. It should not, however, be used by itself to indicate either operation or the operative technique to be used, and it cannot replace clinical examination, which will indicate the treatment of choice. Radiological examination aims only at facilitating the decision by providing complementary information. It can help by preventing useless arthrotomies; by removing any doubt in questionable cases; by confirming the presence of a lesion diagnosed clinically; by defining its site, nature, and extent; by ascertaining the integrity of a meniscus or detecting its defect; and by preventing by an early operation the sequelae of articular traumas.

INDIA

Sensitivity of Vibrio Comma to Antibiotics.—D. C. Lahiri and co-workers (*Indian Journal of Medical Research*, July, 1956) tested 166 strains of Vibrio comma, isolated from a recent epidemic in Calcutta, for their sensitivity to different antibiotics. The organisms were grown from specimens of feces collected during the acute stage of the disease and tested with crystalline penicillin G, dihydrostreptomycin sulfate, tetracycline hydrochloride, chlortetracycline, and chloramphenicol. Results were read after incubation for 20 to 22 hours at 37 C (98.6 F). In general, for their inhibition the organisms required much higher concentrations of crystalline penicillin G and dihydrostreptomycin than of the other antibiotics. Each of these, however, showed a wide range of concentrations between which the most sensitive and the least sensitive strains showed susceptibility. The concentration of a given antibiotic at which all the strains were completely inhibited was 50 to 100 times that at which only the most sensitive strains were completely inhibited. All the strains isolated during this epidemic belonged to the Inaba type. These organisms, isolated during a short space of time, might have been expected to be uniform so far as their antibiotic sensitivity was concerned, but this was not the case. This suggests great diversity in the sensitivity to antibiotics of strains of V. comma. Such a diversity makes precise treatment of cholera with antibiotics a formidable task.

Effect of Sodium Ions on Local Anesthetics.—Y. K. Sinha (*Indian Journal of Medical Research*, July, 1956) studied the effects of local anesthetics on the rectus abdominis muscle of the frog, rabbit and guinea pig ileums, and preparations of cat tracheas immersed in solutions containing different concentrations of sodium ions. The drugs studied were procaine hydrochloride, cocaine hydrochloride, dibucaine hydrochloride, and acetylcholine chloride. It was found that low concentrations of sodium ions in Ringer's solution enhance the antiacetylcholine action of procaine and cocaine on the striated muscle of the frog. High concentrations exert the opposite effect. Low concentrations of sodium ions in Tyrode's solution also enhance the antiacetylcholine action of procaine on the rabbit, guinea pig, and cat smooth muscle; cocaine and dibucaine, however, exhibit a pronounced potentiating effect on the acetylcholine response. Excess of sodium ions might decrease the hydrolysis of salts of procaine and cocaine, thereby reducing their effects, or these drugs might compete with the sodium ion and thus prevent its entry into the muscle cell membrane.

Nutritional Edema.—P. S. Venkatachalam and co-workers (*Indian Journal of Medical Research*, July, 1956) state that nutritional edema is primarily due to protein deficiency during the they can enter the intima. When deposition has already taken place, heparin, via lipoprotein lipase, may be able to split up the lipoproteins in the plaques themselves. Heparin is indicated also in hyperlipoproteinemia in those without arteriosclerosis.

Swiss Medical Profession.—In the winter 1955-1956 there were 3,119 medical students in Switzerland, of whom 1,275 were foreigners, mostly from America. In the last five years, 253 Swiss students of an average age of 27 years have qualified as physicians. There are 7,368 licensed physicians in Switzerland (about 2,322 of whom are specialists) and about 4,500,000 inhabitants. In addition, there are 2,232 assistant physicians in hospitals. Of the 7,368 licensed physicians, 902 are women. Every year about 170 physicians start in private practice, and, of these, 60% are specialists. The average age of physicians at death in Switzerland increased from 64 years in 1945 to 68 years in 1955.

UNITED KINGDOM

Medical Education.—The educational number of the *British Medical Journal* (Sept. 1, 1956) has an annotation comparing American and British medical education. It concludes with the statement that all over the world there is a deep dissatisfaction with the content and methods of medical education. This is expressed not only by the graduates in medicine but progressively and more insistently by the teachers themselves. According to Dr. Morgan Jones, tinkering with the curriculum, patching it here, adding to it there, and scarcely ever removing the useless parts, will no longer suffice. The general medical council is criticized for being too rigid and detailed in its recommendations, which have come almost to have the force of regulations. Its present policy tends to frustrate experiment and perpetuate outmoded methods of teaching. The council will no doubt take heed of these criticisms and consider the many remedies that have been suggested by men of experience and wisdom. Those who from different standpoints and in different countries have thought hard and long about medical education all agree that it must be conducted in universities, not in technical schools.

Prevention of Tetanus.—The *British Medical Journal* of Aug. 11 in an editorial says that during World War I the introduction of routine passive immunization for all wounded reduced the incidence of tetanus in a few months from about 8 to 1 per 1,000, later this figure was lowered still further. In World War II active immunization by toxoid was carried out on a large scale in the Allied armies, and the results were remarkably successful. This success is shown in a recent report of the Army pathology advisory committee, which indicates that a person is to be considered actively immunized for a period of six months if he has received two injections of toxoid, the second not less than 6 or more than 12 weeks after the first, and that he is to be considered immunized for a period of five years if he has received three injections of toxoid, the third not less than 6 or more than 12 months after the second. A dose of toxoid should be given immediately to all wounded men regardless of whether they are actively immunized. In addition, tetanus antitoxin should be given as soon as possible after wounding to any nonimmunized person; its administration should be repeated at seven-day intervals, at the medical officer's discretion. In peacetime, a booster dose of toxoid for all actively immunized persons is recommended every five years. The application of these rules would practically stamp out tetanus.

At present, active immunization of the civilian population in Britain is casual. Apart from the difficulty of deciding whether a particular wound requires an antitoxin, there is the danger of reactions to horse serum after passive immunization. An inquiry at 37 hospitals revealed that 31 were still using the intradermal test of skin sensitivity as a guide to general or constitutional sensitivity, although this test is recognized to be unsatisfactory. Dr. N. H. Moynihan investigated the practical outcome of this test on a series of 8,900 patients and found that, of these, 1,027 (11.5%), who were judged to need prophylaxis were not given it because the intradermal test was positive. A further 293 did not receive prophylactic antitoxin for other reasons: 140 because they had had a previous injection within a period of 3 weeks to 18 months and were erroneously deemed to be sufficiently protected; 70 because of a personal or familial history of allergy, 24 because a general reaction followed a sensitivity test dose; and 59 because they refused.

It is now known that effective protection following a dose of 1,500 units lasts for less than four weeks and may be as short as three days in patients who have had a previous injection. When it was found that these so-called positive skin tests formed such a high proportion of the total, Moynihan carried out two further investigations, using isotonic sodium chloride solution as a control against the test dose of antitoxic serum in one series of 100 patients and tap water in another. The isotonic sodium chloride solution and the tap water produced a reaction similar to that with antitoxin in 47% and 28% of the patients respectively. All 200 patients were subsequently given the full dose of prophylactic antitoxin, and only 4.5% developed serum sickness and 5.5% a localized reaction at the site of injection. The method of intradermal testing for sensitivity to horse serum, which is at present used in many hospitals, is unreliable and should be replaced by the trial dose method. This consists in preliminary subcutaneous injections of a small dose of serum with a view to testing the patient's general reaction before giving a larger dose. Moynihan also draws attention to the fact that previous injection of a soluble antigen leads to a much faster removal from the circulating blood of a second or subsequent injection and consequently curtails the prophylactic effect. He concludes that once a person has received an injection of any horse serum antitoxin, regardless of the disease for which it may have been given, that person should be promptly immunized against diphtheria and tetanus with the appropriate toxoid. This recommendation was not carried out in 36 of the 37 hospitals visited.

Salary Freeze.—The effect of the efforts of the government to halt the inflationary spiral is shown in the comments of a group of general practitioners in Southport, Lancashire. The government has refused even to consider the grounds for an increase in the capitation rate. At a special meeting in August, the practitioners resolved (1) that the action of the government in declining to consider their request for increased remuneration was deplorable, (2) to continue its efforts to obtain remuneration adjusted to current living costs, (3) that if after three months the government had not accepted their recommendation, mass resignation from the National Health Service should be called for, and (4) that, in order that this situation should never arise again, an annual assessment and adjustment of remuneration should be made.

Rockefeller Foundation Grants.—The Rockefeller Foundation has recently announced the following grants to support research work in Britain and the Commonwealth. A grant of $47,600 has been made to the London School of Hygiene and Tropical Medicine for research on the biological value of proteins in tropical foodstuffs. The object of this research is to make it easier to attack the problem of protein malnutrition in tropical countries. The University of Cambridge is to receive a grant of $42,000 to inaugurate a research program in animal psychology. The Walter and Eliza Hall Institute of Medical Research in Melbourne, Australia, where basic research is being done on the nature of viruses, has received financial support from the Rockefeller Foundation since 1934, and the latest grant of $60,000 is to cover an eight-year period. A grant of $10,000 is being made to the Florence Nightingale International Foundation in London toward the expenses of a conference on the planning of nursing studies.

Eyes Offered to Save Sight.—Miss Pat Hornsby-Smith, parliamentary secretary for the Ministry of Health, stated that the ministry could not take advantage of the offer a number of people had made to give in their lifetime one of their eyes to help save the sight of other persons who would otherwise be completely blind. The law on the matter is not certain, but it is possible that a surgeon's deliberately removing a sound eye from a living person, even with that person's consent, might be held to be a criminal offense. In any case it seems most unlikely that surgeons would be willing to perform such an operation. Arrangements for supplying the hospitals that carry out corneal grafting with eyes derived from patients who have died in hospitals are, however, being improved.

CORRESPONDENCE

INTERNSHIPS

To the Editor:—In the Aug. 25, 1956, issue of The Journal, I note that the House of Delegates passed a resolution to the effect that the Council on Medical Education and Hospitals be requested to discourage straight internships in all hospitals. At the Buffalo General Hospital, we have 18 rotating, 3 straight medical, and 3 straight surgical internships. Our staff has good reason to believe that the straight medical or straight surgical internships are superior for certain young graduates who have already had certain house staff experience. It is also our opinion that the type of internship should not be regimented or restricted, and, particularly, those hospitals whose primary objectives are the care of the patient, teaching, prevention of disease, and research should be left to do their own thinking. We in the field of hospital and medical care and medical education are keenly aware of and deeply grateful for the fine job being done by the Council on Medical Education and Hospitals, but we do not believe that the Council would desire or should be expected to carry out this function that it is now being subjected to.

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DEVELOPMENTAL DEFECTS

To the Editor:—The July 14, 1956, issue of The Journal contains an article by T. H. Ingalls (page 1047) on causes and prevention of congenital defects that, I feel, should not go unchallenged. It is the biologist's lot to investigate conditions of living organisms as they exist; even when he experiments, he only produces new constellations of preexisting factors and reactions. The biologist, and with him the medical scientist, cannot choose what fits his hypothesis and relegate the rest to convenient oblivion. Thus, it is difficult to agree with Dr. Ingalls that embryology should logically (or in any other way) precede genetics in the study of abnormal development. The more we learn about these fields, the less we can separate them or let one precede the other; the interested reader is referred to Waddington's "Principles of Embryology" (London, George Allen & Unwin, Ltd., 1956). The disregard of the importance of the ever-present action of genetic factors in all living organisms culminates in Dr. Ingalls' attitude toward the danger of mutations induced by modern sources of radiation. Against his statement that there is no substantial evidence of mutations produced by the atomic bomb in Hiroshima, one may hold (1) that no such evidence could possibly be expected to arise within a decade and (2) that an increased mutation rate has been demonstrated to occur after exposure to ionizing radiation in many organisms. It is interesting to see one man call the danger of mutations a macabre speculation, while 400 leading geneticists from all over the world pass a unanimous resolution that "the damage produced by radiation on the hereditary material is real and should be taken seriously into consideration" (News of Science, *Science* 124:358, 1956). One of the prominent features of mutations is that nothing can be done about them once they have occurred; this should qualify them eminently for a concerted effort of prevention.

The last few decades have seen a spectacular rise of scientific knowledge of abnormal development. By studying the actual sequence of developmental processes descriptively and experimentally, we have learned that the mechanisms entering into the formation of congenital defects are as numerous and varied as are those known in pathology of the adult. Owing to this variety, it is almost always impossible to figure out retrospectively the course of events on the basis of the final form seen at birth. Yet, Dr. Ingalls has availed himself of one "experimental model," the effect of hypoxia on mouse embryos, in order to explain all malformations. The sequence of events leading to abnormalities in these hypoxic mice has, as far as published records go, not been investigated by actual observation. We are led to believe implicitly, if not explicitly, that other teratogenic agents produce a stress equivalent to that of hypoxia and that all that matters is the timing of the event during embryonic life. How are we to reconcile this with much more thorough studies of malformations due to various chemical agents, vitamin deficiencies, and other insults, which can be produced in characteristic form by one or a few agents and never by others, regardless of timing? It may be very tempting to find an answer as simple as that given by Dr. Ingalls. But we can accept it no more than we would believe a statement that all diseases are caused by bacteria just because this was found to be true in one group of cases.

While we may not accept the simple and all-inclusive explanations offered by Dr. Ingalls, we should realize that here is a field as intricate and challenging as any in biology and medicine. From investigations of the actual happenings in abnormal development, and relevant information from many other disciplines, a body of knowledge is bound to evolve that will enable us to approach the goal for which Dr. Ingalls and I and many others strive, namely, the prevention of congenital abnormalities.

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BIRTH OF TWINS

To the Editor:—In the Sept. 15 issue of The Journal, page 229, in Foreign Letters, is a report entitled "Twins Born Twelve Days Apart." In Canada, last year, there was a report of a "second child born 48 days after twin" (*Gazette*, Montreal, March 22, 1955), which, it was alleged, was "the second largest interval between the birth of twins on record. The longest known delay was 56 days." Of interest, therefore, is an authentic case in the Talmud of an interval of three months, and both not only were born alive but later were among the rabbinical authorities cited in the Talmud and known as "Judah and Hezekiah, the sons of Hiyya." Also of interest is the opinion expressed in the Talmud on the still controversial question of superfetation versus superfecundation. The present consensus among embryologists is, I believe, that, where a second child has been born a considerable time after the first and where both are fully developed, it was merely a twin pregnancy in which the second child had been slow in developing, because of a diminished blood supply or for some other cause. It is therefore noteworthy that this is also the opinion expressed in the Talmud.

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SYNTHETIC OXYTOCIN

To the Editor:—In Foreign Letters in the Aug. 4 issue of The Journal, page 1410, under United Kingdom, appeared an item entitled "Synthetic Oxytocin" that is open to some misinterpretation. The impression is given that the oxytocin used in the investigations described was synthesized by the method of du Vigneaud. It is clearly stated by Bainbridge, Nixon, Schild, and Smyth (*Brit. M. J.* 1:1133, 1956) and by Francis and Francis (*Brit. M. J.* 1:1136, 1956) that the material was synthesized by a new method worked out by Boissonnas, Guttmann, Jaquenoud, and Waller (*Helvet. chim. acta.* 38:1491, 1955) and investigated pharmacologically by Konzett, Berde, and Cerletti (*Schweiz. med. Wchnschr.* 86:226, 1956) in the Sandoz Research Laboratories in Basel.

Dr. B. Berde
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MEDICAL FILM REVIEWS

Surgical Treatment of Dissecting Aneurysms: 16 mm., color, sound, showing time 19 minutes. Prepared in 1955 by Michael E. DeBakey, M.D., Denton A. Cooley, M.D., and Oscar Creech Jr., M.D., Baylor University, Houston, Texas. Procurable on loan from Michael E. DeBakey, M.D., Baylor University College of Medicine, Texas Medical Center, Houston 25, Texas.

In this film, consideration is first given to the pathological features of dissecting aneurysms, with the demonstration effected by means of colored drawings of the characteristic pathological changes and the course of events that usually takes place in such a lesion. Two cases are presented, illustrating the two most common forms of the disease: (1) the type in which the dissection begins in the ascending aorta and (2) the type in which the dissection begins at or below the level of the left subclavian artery. The clinical manifestations and diagnostic features for both conditions are presented. This is an excellent film from virtually all standpoints. Use of the schematic drawings is handled well, and the x-rays are presented with remarks that clearly delineate the lesions. While the ingenious surgical technique should be of great interest to the vascular surgeon, the general practitioner should also be exposed to this teaching film chiefly because of the lucid description of the early symptoms and the necessity of early diagnosis and immediate action.

Operative Cholangiography: 16 mm., color, sound, showing time 17 minutes. Technical Advisors: Philip F. Partington, M.D., and Maurice D. Sachs, M.D., Cleveland. Produced in 1955 by and procurable on loan from Central Office Film Library, Veterans Administration, Washington 25, D. C.

The purpose of this film is to illustrate the technique of cholangiography and its advantages to the surgeon, radiologist, x-ray technician, and anesthetist. The authors deviate slightly from the usual routine of cholangiography, insofar as they observe the pressure in the common duct by means of a ureteral catheter in the cystic duct while they are injecting the Diodrast into the common hepatic duct. They use a concentration of Diodrast varying between 10 and 70%, depending upon the size of the common duct. They do not inject the Diodrast with a pressure greater than 20 cm. H_2O. Five cubic centimeters is injected and a roentgenogram taken. Two additional injections of 5 cc. are made, followed by taking of an x-ray film. If the common duct is opened to remove stones, a double-lumen T-tube is inserted and the process of injecting Diodrast and taking films is repeated to find out whether any stones have been left in the duct. The authors claim that this procedure will require little additional time. Since they are actually taking three to six films, one might question this statement. Almost certainly the method described would necessitate a lot of experience and almost full-time use of an x-ray technician in order for a large hospital to use the technique without loss of much time. The authors have expressed their points quite clearly. The only question that arises centers around the question as to how convinced one is that operative cholangiography is necessary as a routine procedure. The photography and animation are excellent. The film is well organized and concise and is very well done.

The Search: Johns Hopkins University (Deafness): 16 mm., black and white, sound, showing time 26 minutes. Produced in 1955 by CBS Television. Procurable on lease (10 years, $125) or rental ($5) from Young America Films, 18 E. 41st St., New York 17.

This film deals with a new approach to the diagnosis and treatment of deafness in children that is based on the theory that there is rarely, if ever, a total loss of hearing. The biggest stumbling block in the past has been determining what percentage of hearing exists in young children who have not yet learned to communicate and who, yet, should begin a training program as early as possible. The procedures of the hearing and speech center at Johns Hopkins University in Baltimore are explained by Drs. William Hardy and John E. Bordley as a 2½-year-old child undergoes preliminary tests to determine the extent of his hearing. The film also shows how children with hearing disabilities can lead full and useful lives if their hearing loss is detected and measured early enough and if they embark immediately on a guided training program. Children in various stages of training are shown. Near the end of the film it is mentioned that hearing loss is measured in decibels, but it is not specified where that loss is in the spectrum. It would be better to say 70-db. loss in the speech range. This film will be of interest to lay groups, particularly to mothers of children who have some hearing loss.

Magic of the Atom Series: 16 mm., black and white, sound. Produced in 1955 by and procurable on loan ($10 each) or purchase ($55 each) from Handel Film Corp., 6926 Melrose Ave., Hollywood 38, Calif.

Atoms for Health: Showing time 12 minutes.

The first part of this film illustrates a test of the ability of the liver to remove foreign substances from the blood stream. Radioactive albumin is injected into the blood stream to indicate, on a recording chart, the amount of blood flowing to the liver. When this registers, rose bengal is injected to carry additional radioactive iodine to the liver. The second part of the film shows a demonstration of the Theratron, a new cobalt source used in science's fight against cancer. A complete case history is followed, step by step. This is extremely interesting, inasmuch as physicians who visit cobalt-60 installations are not always privileged to see the actual rotation of the unit. The film is recommended for showing to lay audiences and also to physicians. The photography and narration are excellent.

Atomic Biology for Medicine: Showing time 12 minutes.

The purpose of this film is to show atomic biomedical research with animals, including the effect of radiation on the eyes, cell division, bones, and tumors. Dust inhalation studies are also described. This film is extremely valuable because of the wealth of technical effect implicit in every sequence. It is instructive to contemporary audiences who may not actually have seen the machining of uranium and the injection of radioactive beads into a tumor; it will be very valuable to future audiences as a documentary of 1955 techniques. The photography and narration are excellent, and the film is recommended for college biology classes and to medical audiences seeking to inform themselves about the use of radioactive preparations in medicine.

Hemipelvectomy, Interilioabdominal Amputation: 16 mm., color, sound, showing time 23 minutes. Prepared by George T. Pack, M.D., and Theodore R. Miller, M.D., New York. Produced in 1955 by Sturgis Grant Productions, New York, for and procurable on loan or purchase ($125) from E. R. Squibb & Sons, Division of Olin Mathieson Chemical Corp., 745 Fifth Ave., New York 22.

The purpose of this film is to show the authors' technique for performing a hemipelvectomy, involving interilioabdominal amputation, for a large rhabdomyosarcoma in the left femoral trigone. The patient shown is a 44-year-old female who had previously been admitted to a hospital with a lump in the left femoral trigone. A biopsy was done; the unencapsulated and diffusely infiltrating tumor was reported to be a rhabdomyosarcoma. Because of the size, fixity, invasive nature, histogenesis, and location of the tumor, it was decided that hemipelvectomy be done. The patient is shown three months after the operation, learning to use her artificial limb. She is able to sit comfortably and to walk with one cane; the scar is shown to be well healed. The technique of hemipelvectomy is well demonstrated, and the film in general is excellent. The film concludes with a review of two patients walking in a prosthetic device that has been devised for this type of patient. The patients walk very well; however, they are in the younger age group, and possibly this is a little exaggeration of what the usually more elderly patient can do. This film is recommended for specialists and those surgeons who are interested in this procedure.

Scare Story—A True Story About Hospitals: 16 mm., color, sound, showing time 16 minutes. Produced in 1955 by Impact Productions, under the sponsorship of the Childrens Hospital of Los Angeles. Procurable on rental ($4) from American Hospital Association, 18 E. Division St., Chicago 10.

This film consists of a prologue, entitled "Scare Story," that is designed to be shown to hospital personnel only. It dramatizes the fears a child might have if not properly prepared for hospital admission. The film, "A True Story About Hospitals," follows a boy and girl from the time they first meet the admitting clerk through their whole hospitalization. Through the children's eyes, the audience comes into contact with the x-ray camera, intravenous feeding, an oxygen tent, blood tests, anesthesia, and the operating room. By the time the children are ready to go home, they have witnessed almost all the ordinary hospital procedures. This is an excellent film for the orientation of children to the hospital experience; it will be particularly valuable where the services of a local hospital approximate those shown in the film so that the experiences can be comparable. However, the prologue is unnecessary and should be removed. This film will also be of value is acquainting hospital personnel, including physicians, with some of the attitudes and behavior toward children in the hospital situation.

THE LEISURE CORNER

THE LOS ANGELES DOCTORS' SYMPHONY ORCHESTRA

Creating music interpretatively together with others provides a satisfaction over and above that found in just listening to good music. The members of the Los Angeles Doctors' Symphony Orchestra and of doctors' orchestras in other cities have found that playing in the orchestra provides good fellowship and aids in promoting culture in the community.

The Los Angeles group finds that these activities play an unusual public relations role, by revealing another important side of the doctor. Direct assistance to worthwhile medical causes is rendered by playing benefit performances; this orchestra generally plays two each year: one in the winter for its permanent beneficiary, the Los Angeles County Physicians Aid Association, and a second in the spring for different beneficiaries. A highlight of the forthcoming third annual formal concert will be the appearance of Mr. Donald O'Connor, who will be guest conductor of a symphony he is writing for a movie that he expects to produce. This concert, for Physicians Aid, will take place at the Los Angeles Philharmonic Auditorium on Jan. 12, 1957.

The orchestra has just started its fourth season. There are 90 members, mostly M.D.'s, with a fair representation of dentists, veterinarians, chiropodists, and physicians' wives. General practice and virtually all medical specialties are represented. The largest group of members are psychiatrists. While most of the positions are filled, several openings exist, particularly in the cello, bassoon, and English horn sections.

This orchestra has enjoyed the good fortune of having Mr. William Van den Burg as conductor and music director since its inception. Mr. Van den Burg combines the rare talents of fine musicianship and the diplomacy that is essential to weld so many "rugged individualists" into a professional-sounding ensemble. He is currently principal cellist at Universal Studios and formerly was principal cellist and assistant conductor with Stokowski, Monteux, and Wallenstein. After the weekly rehearsals in a Hollywood junior high school, a number of the orchestra members can be found relaxing over coffee in a restaurant near the famous corner of Hollywood and Vine. As might be expected, most of the discussion concerns medicine and music.

Benjamin Gross, M.D., of North Hollywood, concertmaster of the orchestra, was formerly concertmaster of the Louisville Symphony Orchestra and is now a rare combination of pathologist and psychiatrist. The president is Jerome M. Kummer, M.D., a Santa Monica psychiatrist, who is also principal in the bass violin section. Dr. Arthur M. Grossman, vice-president, plays the flute; he practices pediatrics in Beverly Hills. Jack Fields, M.D., an ophthalmologist from North Hollywood, occupies the principal chair in the trumpet section and is secretary-treasurer. Mrs. John (Shirley) Brody, librarian, plays in the viola section; her husband, a Beverly Hills anesthesiologist, is a cellist with the orchestra.

There are several ex-professional musicians in the orchestra. In addition to Dr. Gross, there is M. Richard Ferguson, M.D., principal trombonist, who formerly played with name bands, the last one being Stan Kenton's. Dr. Ferguson practices orthopedics in Santa Monica. Dr. Samuel Hoffman, the only chiropodist in the orchestra, plays in the first violin section and has the distinction of being the only member who does some professional work in music. He plays the theremin, an unusual instrument that produces an unusual tone electronically; the pitch is controlled by the player never touching the instrument, but moving his hands near it. Dr. Hoffman has played the theremin in many film sequences. He will long be remembered for his performance during the dream sequel in the film "Spellbound."

Through the years The Journal has published news items concerning doctors' orchestras in New York, Detroit, Akron, St. Louis, Chicago, Washington, D.C., San Francisco, and Los Angeles. The Akron doctors' orchestra, under the able leadership of its director, Dr. A. S. McCormick, has just completed its 30th season, having given 193 concerts in that time. In addition to doctors' orchestras, there are numerous smaller groups of physicians devoted to the better known works of chamber music, and some to the still better known works of Dixieland jazz. Much has been theorized on the attraction of doctors toward music and the relationship between medicine and music. It is possible that this was recognized by the ancient Greeks, since Apollo, the god of music, was the father of Aesculapius, the god of medicine.

No statement from the Los Angeles Doctors' Symphony Orchestra can be considered complete without a tribute to its impressario, Dr. Elizabeth Mason Hohl, president of the Physicians Aid and liaison officer with the Los Angeles County Medical Association, whose officers and staff have always proved of great assistance.

Los Angeles Doctors' Symphony Orchestra, William Van den Burg conducting.

collagen diseases, they seem to occur more frequently in patients with these diseases than in other people of the same age. Therefore, the coexistence or future development of a malignant tumor should always be considered in this group of patients.

Gastric Biopsy in the Megaloblastic Anaemias. J. L. Markson and W. M. B. Davidson. Scottish M. J. 1:259-266 (Aug.) 1956 [Glasgow, Scotland].

The introduction of a flexible suction gastric biopsy tube by Wood and his colleagues in Australia made available a simple and relatively safe method of obtaining fragments of the gastric mucosa for histological study. Markson and Davidson describe the histological appearances of gastric samples taken from patients with pernicious anemia and other megaloblastic anemias. Biopsy revealed gross atrophy of the gastric mucosa in all 16 patients with pernicious anemia. Minor inflammatory changes were found in four of the cases of gastric atrophy. In two of the remainder, thickening and fibrosis of the muscularis mucosae, indicative of previous inflammation, was present. Normal mucosa was found in four patients with megaloblastic anemia of pregnancy. Of three patients with megaloblastic anemia and idiopathic steatorrhea, one had normal mucosa and two had atrophic gastritis.

The histological findings in pernicious anemia were compared with those obtained in iron-deficiency anemia and in a series of nonanemic hospital inpatients. The abnormalities of the gastric mucosa were not diagnostic and did not differ materially from severe lesions encountered in the other two groups. The lack of diagnostic information yielded by gastric biopsy and the real, though slight, risk of hemorrhage limit the value of the procedure in the diagnosis of doubtful cases of pernicious anemia and of subacute combined degeneration of the cord. Since the gastric mucosa is nearly always grossly abnormal in histamine-fast achlorhydria, it is safer and almost as useful to rely on the result of the histamine test meal. The histological evidence obtained by gastric biopsy strongly suggests that there is a gradation from normal mucosa through superficial and atrophic gastritis to gastric atrophy. This sequence of events is not necessarily an invariable occurrence in pernicious anemia, in which gastric atrophy may also occur as a genetically determined characteristic.

Clinical Contribution to the Use of Hyaluronidase in the Treatment of Edema and Ascites. Riforma med. E. Bellis and M. Campilonzo 70:907-910 (Aug. 11) 1956 (In Italian) [Naples, Italy].

The authors treated 10 patients with edema and ascites with hyaluronidase. Four patients had cirrhosis of the liver, five had heart disease, and one had nephritis. The drug was given by subcutaneous, intravenous, intramuscular, and intraperitoneal routes. Subcutaneous and intramuscular injections gave poor results and were abandoned after preliminary experiments. Doses given intravenously consisted of 500 units daily every day for a period of from 5 to 15 days. Three patients received intraperitoneal injections of 1,000 units every other day for four days. The diet was kept normal. The urine was tested. The circumference of the abdomen was checked. Hyaluronidase had a very good effect on patients with relatively good circulation. Intravenous injection was the best method of administering the drug. Intraperitoneal injections gave poor results in patients with ascites. Diuretic substances improve the effect of hyaluronidase. The drug was well tolerated by all patients.

A Clinical Study of Scrub Typhus in North Queensland. R. L. Doherty. M. J. Australia 2:212-219 (Aug. 11) 1956 [Sydney, Australia].

This report is based on a series of 53 patients with scrub typhus studied at a station of the Queensland Institute of Medical Research from March, 1953, to November, 1954. Rickettsia tsutsugamushi was isolated from 45 of these patients by mouse inoculation. Proteus agglutination tests were performed on paired serums from all patients and confirmed the diagnosis in the eight cases in which no strain was isolated. The clinical picture was milder than that described in preantibiotic Queensland series, although several patients had severe illnesses. Lymph-node enlargement, rash, and eschar were the commonest findings on physical examination. Several points of correlation could be demonstrated between the clinical picture and the virulence of the causative organism in mice. The course of the disease reflected the influence of treatment, especially in the total duration of fever. Forty-five patients were treated with chloramphenicol, two with tetracycline, and one with chlortetracycline. The results were satisfactory, but in seven the response was less rapid than expected. Nine patients had relapses after responding to treatment. Seventeen patients did not develop agglutinins against Proteus OXK, and in seven others a diagnostic titer was not reached. The factors that may have influenced this are discussed, and some evidence is presented that mild strain infections, treated with an effective antibiotic early in the illness, are more often OXK-negative.

The Use of Butazolidine in Gonococcal Arthritis. N. P. Burns. M. J. Malaya 10:313-319 (June) 1956 [Singapore, Malaya].

Gonococcic arthritis is still frequent in the Ulu Kelantan district in Malaya, where gonorrhea is still prevalent. Burns reports observations on 15 patients with this form of arthritis. The interval between acute urethritis and gonococcic arthritis varied from two weeks to several years. The arthritis may be monoarticular or polyarticular. In a typical case the onset is explosive, with two or three large joints becoming hot, swollen, and tender, with mobility reduced by pain, often of excruciating severity. Many of the other joints, although not hot or swollen, become painful. After a varying interval, usually about one month, the acute stage of the disease settles but the patient is left a semi-cripple as a result of severe pain arising from the periarticular tissues and evoked by movement of the neighboring joint. Pain may also be present at rest. The subsequent course of the disease is one of exacerbation and remission. The 15 patients were men ranging in age between 15 and 40 years. Six had the monoarticular and nine had the polyarticular form of gonococcic arthritis. Symptoms had existed for an average of five years. Treatment had varied from native remedies to high dosage courses of penicillin and other antibiotics. Response to all forms of treatment had been poor. Administration of butazolidine was started with a single intramuscular injection of 600 mg., followed by 400-mg. tablets twice a day for five days. Although the original idea of commencing treatment intramuscularly was for purely psychological reasons, in fact the objective response produced by an injection, as assessed by diminution of swelling, increase in joint mobility, and rapidity of response, was more dramatic than that produced by a comparable dose given orally. Since butazolidine was given not to cure or eradicate the disease but merely to control its symptoms, subsequent therapy was given only when symptoms recurred. When gonococcic arthritis is controlled by intermittent courses of butazolidine, the toxic reactions are few. Butazolidine is a valuable agent in the treatment of gonococcic arthritis and worthy of trial in cases not responding to other methods.

Endocarditis Lenta: A Review of 118 Patients Treated During the Ten-Year Period 1945 to 1954. W. J. Kaipainen and K. Seppala. Acta med. scandinav. 155:71-81 (No. 1) 1956 (In English) [Stockholm, Sweden].

The authors report on 118 cases of subacute bacterial endocarditis treated in the First and Second Medical Clinics of Helsinki University during the period from 1945 to 1954. Positive blood cultures were obtained in 36% of the cases. Unless the blood culture was definitely positive or ulcerative-verrucous endocarditis was verified at autopsy, the following were the criteria governing the selection of the material: (1) valvular disease or congenital heart disease, (2) prolonged fever, (3) anemia, (4) focal embolic nephritis, and (5) an increased sedimentation rate.

The patients were divided into four groups: (1) 18 who received sulfonamide treatment or no antibacterial treatment at all; (2) 39 who received penicillin in a total dosage of less than 15 million units each; (3) 21 who received penicillin in a total dosage of more than 15 million units each; and (4) 38 treated with penicillin and other antibiotics. Many of the patients in group 4 received an average of from 1 to 2 million units of procaine penicillin in combination with 1 gm. of tomycin, each in two doses per 24 hours. The total penicillin ge in many cases exceeded 50 million units. Evaluation of esults six months after treatment was started showed a val rate of 0% in group 1, 20.5% in group 2, 67% in group d 68% in group 4. Two additional patients, one of whom treated with a total dosage of 24.5 gm. of streptomycin the other, because of allergy to penicillin, with 32 gm. of mycin, recovered and were living, the first six years and econd two and one-half years after the beginning of the nent. The final mortality rate (after 6 months) was higher oup 3 than in group 4, but whether this was because illin in large doses alone is a poorer therapeutic measure penicillin in combination with other antibiotics is open to ion. The infection in these cases was halted and the nts died of other causes, e. g., exacerbation of cardiac e due to the valvular lesion or cerebral and other emboli. tients with suspected subacute bacterial endocarditis should time be left untreated, even when the blood cultures are ive. The cultures may be negative for one or more technical reasons, and treatment should not be postponed until a ve culture is obtained. The low percentage of positive res obtained in the present series, only 36%, for instance, have been due to (1) too few samples, (2) samples taken ng or immediately after antibiotic treatment, (3) failure of pling technique, and (4) failure of cultivation technique.

xperience in some of these cases showed that the pain of reed intramuscular injections can be avoided by the use of aine penicillin in combination with streptomycin; in others, im treatment with tetracycline preparations was given for, a week without untoward effects. Antibiotics should be n prophylactically to patients with valvular lesions and genital heart lesions who are to undergo dental or surgical edures usually accompanied by the temporary liberation of eria into the bloodstream.

of Radioactive Iodine for Intractable Angina Pectoris. A. M. lman. J. Louisiana M. Soc. 108:337-343 (Sept.) 1956 [New ans].

oldman reports observations on 13 euthyroid patients who e treated with radioactive iodine (I^{131}) for angina pectoris r all conventional forms of therapy had failed. Seven of the ents were women and six were men, their ages ranging from to 79 years. A tracer dose of $50\mu c$ was used, and the uptake measured at a distance of 17 cm. directly over the gland. rmal uptake of I^{131} is considered to be between 10 and 40% the tracer dose in 24 hours. A single large therapeutic dose s used in all 13 patients, because it was desired to shorten period of irradiation and secure an earlier onset of hyporoidism. This single dose resulted in postirradiation thyroid-, release of large amounts of thyroid hormone, and exacertion of the patients' symptoms. Since this course has proved wise, future patients will be treated with divided doses.

Five of the patients died, three from acute myocardial inction, one after the development of acute pulmonary edema, d one from cerebrovascular accident. A lymphoblastic lymoma developed in one patient nine months after administraon of the treatment dose. It is interesting to note that this tient has several sisters and brothers with malignant disease. he follow-up period of the eight surviving patients now varies om two to five years. The effect on the angina was excellent five of the eight survivors, good in one, and fair in two. The set of clinical improvement coincided with the appearance f signs of myxedema. No toxic effects were noted on the hemaopoietic system or the kidneys. The surviving patients are being naintained on minimal doses of thyroid extract to prevent clinical myxedema. The favorable results obtained in the survivors seem to warrant further careful study of this method of relieving intractable heart disease.

Eyeball Bruits. J. H. Cohen and S. Miller. New England J. Med. 255:459-464 (Sept. 6) 1956 [Boston].

Eyeball bruits were discovered in seven patients admitted to the medical service of a 370-bed general hospital during a two-year period. Two cases were proved, and one was suspected, to be due to arteriosclerotic narrowing of the carotid siphon. One case was proved to have been caused by internal carotid artery thrombosis in the cavernous portion. The bruit was bilateral in the remaining three cases, one of which was due to hemangioma and the other two to profound anemia. The quality of the bruits was similar in all seven patients, but their intensity varied from patient to patient and also from time to time in the same patient. All the bruits were synchronous with the heartbeat and were systolic in time. They could be made to disappear by pressure on the ipsilateral common carotid artery. The sound itself was a soft blowing murmur, and before it could be heard the stethoscope often had to be placed with just the right amount of pressure and the patient had to be asked to hold his breath while either the examiner held the other eye closed or the patient opened it. Sounds that were inaudible over the orbital bones or other nearby structures could often be heard when the stethoscope was applied to the eye itself. Auscultation should therefore routinely include the application of the stethoscope to the eye itself, sepecially in cases of neurological or circulatory disease in which no bruit can be heard over the cranium. The examination should be made with the patient in the sitting and the supine positions, as well as lying on each side.

The relative frequency of eyeball bruits, especially those caused by occlusion and narrowing of the cavernous portion of the internal carotid artery, suggests that auscultation of the eyeball itself will often supply valuable information in the diagnosis of cerebrovascular diseases and that it should be more widely used.

Progressive Pulmonary Dystrophy: Vanishing Lung (Burke), Idiopathic Pulmonary Atrophy (de Martini). L. Heilmeyer and F. Schmid. Deutsche med. Wchnschr. 81:1293-1297 (Aug. 17) 1956 (In German) [Stuttgart, Germany].

Heilmeyer and Schmid are concerned with a pulmonary disorder that they feel should be differentiated from the different forms of pulmonary emphysema or pulmonary cysts, the more so since the pulmonary destruction goes deeper than in the case in the ordinary substantial pulmonary emphysema and involves not only the peripheral pulmonary tissues but also the proximal parts of the pulmonary vessels and of the bronchial tree. The lesions are usually not diffuse but involve only one lobe of a lung. Similar cases were formerly described under the general heading of pulmonary emphysema. Crenshaw spoke of "vanishing lung" or "cotton candy lung." Burke in his first description of "vanishing lung" believed that the process was an emphysema with vesicles of enormous size so that a gigantic emphysema vesicle might eventually fill an entire lobe. In Italy cases were described by de Martini, who differentiated them from the various forms of emphysema as well as from pulmonary cysts and who spoke of idiopathic pulmonary atrophy. In Germany cases of this type were usually described under such terms as pulmonary cysts or spontaneous pneumothorax.

The five patients whose histories are presented all had pulmonary lobes or parts of lobes in which the pulmonary tissue, including the proximal portions of the bronchi and vessels, had been completely destroyed. This destruction may produce cyst-like cavities, as was the case in two of the patients. In three of the patients who were observed over a number of years and in whom roentgenograms were made repeatedly, the condition was definitely progressive, whereas it remained constant over 15 years in the first case. The progressiveness of the process in three of the patients differentiated the condition from idiopathic pulmonary atrophy as described by de Martini, and for this reason the authors prefer the term "progressive pulmonary dystrophy."

Pulmonary or bronchial infections existed at the onset in four of the patients. Two of these also smoked excessively and another patient worked with tobacco. The abuse of nicotine as a possible causal factor was also mentioned by Crenshaw, who, moreover, was of the opinion that the destruction of the lung was caused by obliteration of the bronchial and pulmonary arteries. This simultaneous occlusion of the bronchial and pulmonary arteries is also regarded as an important factor by the authors. They believe that an inflammatory endarteritis obliterans is one of the primary causes and suggest that infection of the lung leads to sensitization of the vessels. Pulmonary dystrophy would then be the sequel of a Buerger's disease of the pulmonary and bronchial arteries. The frequent concurrence of infection with severe abuse of nicotine would fit into this concept. As regards treatment, attention should be given to the accompanying infections because these may favor further progression of the pathological process. Crenshaw is of the opinion that surgical therapy would be advisable, particularly after the atrophic pulmonary tissue loses its elasticity and the bullous emphysema causes compression of the healthy portions of the lung. This may apply particularly to processes characterized by emphysema with enormous vesicles and perhaps also to patients with pseudocysts. The authors believe, however, that in the purely dystrophic form without compression of the surrounding tissue surgical treatment is not indicated, unless it can be proved that the exclusion of the inflammatory process in the dystrophic portion of the lung will arrest the progress of the disease.

Idiopathic Ulcerative Esophagitis: Report of a Case. H. Achenbach, J. P. Lynch and R. W. Dwight. New England J. Med. 255:456-459 (Sept. 6) 1956 [Boston].

Idiopathic ulcerative disease primary in and confined to the esophagus appeared in a 25-year-old man first seen because of tenderness and discharge in the anal region. He had had recurrent episodes of tenderness in that region relieved by spontaneous drainage for more than a year. The first such episode had occurred during service in Korea. The patient was well developed and had no physical defects except one abscess and three fistulous openings in the perianal region. Laboratory findings were normal except for a hemoglobin level of 11.5 gm. per 100 ml. Two readmissions for similar complaints took place later in the same year, and on each of these occasions biopsy of a fistulous tract showed granulation tissue with nonspecific chronic inflammation. Migratory arthritis, erythema nodosum, and dermatitis gangraenosa appeared in connection with the persistent multiple perianal abscesses and fistulas. Painless dysphagia, which was the initial symptom of the primary esophageal disease, began nine months after the first hospital admission. Thickening of the longitudinal folds of the esophagus seen on x-ray examination was the first demonstrable esophageal abnormality. The mucosa became fissured and then ulcerated, with undermining and pseudopolyp formation. The esophagus lost its motility and became stenotic and obstructed. Multiple perforations caused abscesses in the upper lobe of the right lung and in the mediastinum. Esophagectomy, performed as a lifesaving procedure, was followed by gradual improvement. Drainage from the anal region subsided spontaneously. The arthritis, erythema nodosum, and gangrenous skin ulcers, which were becoming more severe and widespread despite cortisone and antibiotic therapy, were also resolved. All these have been described as complications of ulcerative colitis, and when they occur this diagnosis must be considered even in the absence of colonic symptoms. The origin of these complications is not understood. They may represent toxicity from a gastrointestinal tract that is more than normally permeable or a decrease in resistance to infection in a chronically ill patient, or they may be an integral part of a disease complex.

The diagnosis of ulcerative colitis was often considered in this patient, but it was never substantiated by barium-enema study or sigmoidoscopy. The curative effect of esophagectomy on the associated conditions was the same as that of colectomy in ulcerative colitis. No similar cases have been found in the literature.

A Clinical Trial of BZ-55. L. J. P. Duncan, J. D. Baird and D. M. Dunlop. Brit. M. J. 2:433-439 (Aug. 25) 1956 [London, England].

Carbutamide (BZ-55) was given a trial in 44 patients over 45 years of age with mild diabetes mellitus who were not overweight by more than 10% of their ideal weight but who, on a fully restricted diet, continued to show significant hyperglycemia and glycosuria and, therefore, required insulin therapy in addition to dietary measures. One group of 22 patients remained in the hospital for 20 days, while a second group of 22 patients was hospitalized for 8 days only. Although most factors were kept constant throughout for all patients, the diets were individually prescribed and the dosage of carbutamide was adjusted according to the clinical response. Treatment was started with 3gm. (six tablets) given by mouth before breakfast in 12 patients and with 4.5 gm. in 32 patients. Blood was withdrawn at hourly intervals for five hours thereafter, and its glucose and carbutamide content were determined. The patients remained in bed and food was withheld during the period of the test. If the response was satisfactory, the dose was gradually reduced over three or four days to 1.5 gm., but if the response was inadequate, 4.5 gm. was given daily for several days. Patients whose response was considered to be clinically satisfactory were discharged on a daily maintenance dose of carbutamide varying from 1 to 1.5 gm.

Sixteen patients in group 1 and 16 patients in group 2 responded well enough to the drug to be classed as clinical successes. Three patients in group 2 responded to the drug but were clinical failures. Nine patients did not respond to continued treatment with carbutamide. In responsive patients who were also clinical successes, the drop in fasting blood glucose was roughly proportional to the fasting blood-glucose concentration in the control period. In the unresponsive patients there was no such relationship. The three responsive patients who were clinical failures occupied an intermediate position. Glucose-tolerance tests showed that carbutamide is without effect on glucose tolerance. The drug was without effect on ketosis or on patients who readily developed ketosis. Follow-up studies of the discharged patients for from 4 to 18 weeks showed that maintenance treatment with carbutamide must be continuous and not intermittent. Minor toxic effects were observed in several patients, and there appears to be a possibility that thrombocytopenia may occur. The difficulties encountered in selecting the responsive patient and the dangers of withdrawing insulin in the unresponsive patient are emphasized. Carbutamide should not be given as a substitute for dietary restriction. When this principle is observed, the number of patients in whom it can replace insulin is more limited than reports to date have suggested.

Trial of an Oral Hypoglycemic Agent in Diabetes. F. W. Wolff, G. A. Stewart, M. F. Crowley and A. Bloom. Brit. M. J. 2:440-445 (Aug. 25) 1956 [London, England].

Thirteen men and 32 women, 6 between the ages of 21 and 40 years, 13 between the ages of 41 and 60, and 26 between the ages of 61 and 80, with diabetes mellitus normally requiring insulin, were admitted to hospital, were given a diet suitable for their physique and metabolic needs, and were maintained on this diet alone without insulin for five days. For the next two days no breakfast was given, but on the second day an initial dose of 2.5 or 3.5 gm. of carbutamide (BZ-55) was given in the morning. Except for the young ones, the patients received a dose of 2 gm. on the following morning, followed by 1 gm. daily for at least five days as inpatients and then as outpatients. In poorly controlled patients, administration of 3 gm. daily was begun on the eighth day and continued for five days. In some patients rapid loss of weight and ketosis necessitated an earlier resumption of insulin therapy, which also became necessary occasionally in those in whom trebling of the dose was attempted.

Nineteen patients were clinical successes and 26, including the 6 young patients, were therapeutic failures. The patients in whom carbutamide was successful frequently had a history of diminishing insulin requirements. In none of these was the fasting blood sugar level greater than 275 mg. per 100 cc., and the fasting range was from 123 to 275 mg. per 100 cc. The patients in whom carbutamide failed tended to have a higher insulin requirement than those in whom it was successful. Their fasting blood sugar levels ranged from 123 to 421 mg. per 100 cc., and they had a tendency to acetonuria. Carbutamide did not exert any influence on the postprandial rise in blood sugar levels, either in the group of successes or in that of failures. There was no difference in levels between free and conjugated sulfonamides in the blood between successes and failures. There was more excretion of conjugated sulfonamides in the urine of the patients in whom the drug failed than in those in whom it was successful. Five patients (11%) had skin reactions to carbutamide. In four of them carbutamide was replaced by N-(4-methylbenzosulfonyl)-N′-butylurea (D860), which has hypoglycemic properties similar to those of carbutamide although it is not a sulfonamide preparation, and the typical maculopapular sulfonamide rash then gradually disappeared.

Myotonia Atrophica with Testicular Atrophy: Urinary Excretion of Interstitial-Cell–Stimulating (Luteinizing) Hormone, Androgens and 17-Ketosteroids. B. G. Clarke, S. Shapiro and R. G. Monroe. J. Clin. Endocrinol. 16:1235-1244 (Sept.) 1956 [Springfield, Ill.].

It has been suggested that dystrophia myotonia (myotonia atrophica) may represent a pluriglandular disturbance of endocrine origin and be susceptible to treatment by endocrine replacement therapy. An alternative interpretation is that, instead of reflecting a primary endocrine disturbance, dystrophia myotonia is simply a manifestation of genetically linked degenerative phenomena seen in various tissues derived from embryonic ectoderm and mesoderm. It has been defined as "a steadily progressive, familial, distal myopathy with associated weakness of the muscles of the face and levators of the eyelids, tendency to myotonic persistence of contraction in the affected parts, and testicular atrophy." The authors found the records of seven patients with dystrophia myotonia in the files of their own hospital, and all had testicular atrophy. They found atrophy of the testes recorded also in 65 of 81 male patients with myotonia atrophic collected from the literature. Detailed clinical, endocrine, and histological studies were carried out on two typical cases. Histological observations on testicular tissue were correlated with measurements of urinary excretions of androgens, luteinizing (interstitial-cell–stimulating) hormone, follicle-stimulating hormone, and 17-ketosteroids.

In the first patient the disease began at the age of 10 years and in the second at 26 years. Muscular weakness and atrophy were local in the first patient, being confined chiefly to head, neck, forearms, and hands, although myotonia was pronounced. In the second patient, weakness and atrophy were generalized and tended to obscure the myotonia. As anticipated, the serum creatine level and urinary creatine excretion were elevated. In both men the testes were small and soft, the size of peas. Biopsy of the testes showed normal or increased interstitial cells in association with atrophy of the spermatogenic tubules. Assays of the urine showed follicle-stimulating hormone to be normal, 17-ketosteroids low, luteinizing (interstitial-cell–stimulating) hormone greatly increased, and androgens greatly reduced. No other evidence of endocrine disturbance was observed. Although there have been reports on endocrine replacement therapy in the form of testosterone propionate, corticotropin, and cortisone in patients with dystrophia myotonica, the results appear to have been poor or equivocal.

Treatment of Eczema Vaccinatum by Specific Gamma Globulin: A Case Report. M. J. Fox and V. B. Pica. Wisconsin M. J. 55:972-976 (Sept.) 1956 [Madison, Wis.].

A 57-year-old man had a severe vaccinia after contact with his 18-year-old daughter, who had had a chronic eczema all her life and who had received a routine smallpox vaccination that was followed by a severe pruritic, macular, papular, and vesicular eruption on her face and body. The father had helped her to the bathroom, had handled her eating-utensils, and had direct contact with her towels and linen. The same vesicular eruption as in the daughter occurred over the face, scalp, and body of the father. On admission, there was edema and pain in the face, marked headache, tinnitus, pruritus, fever, conjunctival injection, photophobia, dryness of the mouth, nausea, malaise, and general arthritic joint pain. The patient was given 30 cc. of vaccinia globulin intramuscularly. Shortly thereafter his temperature returned to normal. Improvement of the eczema vaccinatum was rather rapid, and the patient's condition remained stable until discharge eight days later except for one febrile episode on the day after the vaccinia globulin injection. Vaccinia immune globulin has an important place in the prevention and treatment of serious complications of smallpox vaccination, particularly eczema vaccinatum.

Milkers' Nodules. C. E. Wheeler and E. P. Cawley. South. M. J. 49:973-978 (Sept.) 1956 [Birmingham, Ala.].

Wheeler and Cawley became interested in milkers' nodules in 1952, when they observed two patients with this disease in Virginia. The histories of these two patients and of six others observed later are described. The lesion appears first as a tiny, round, erythematous macule that soon becomes thickened to form a papule and slowly grows until it reaches the diameter of a centimeter or slightly larger. It attains its full size in about four weeks, remains essentially static for approximately two weeks, and gradually resolves without scar formation, the entire course of the uncomplicated lesion taking from six to eight weeks. The mature lesion is usually round, sharply demarcated from the surrounding skin, and dome-shaped. Some of the lesions have a flat or plateau-like top. One or two lesions are most commonly seen, but sometimes six or eight appear. When large numbers of lesions are seen, the disease is usually not milkers' nodules but true cowpox (vaccinia), and laboratory studies will demonstrate the true etiology.

Milkers' nodules appears to be an infectious disease. The disorder almost always appears first in the cow, and man contracts it on the parts most exposed to the lesions on the cow, i. e., on the hands and forearms. The lesions in the cow are variously described by patients and veterinarians as warts, pimples, scabs, crusts, vesicles, and pustules on the teats or udders. Several lesions are usually present, but aside from local soreness the cow is not affected systemically. A viral cause has been assumed for milkers' nodules, and there have been a few reports on inclusion particles in the epidermal cells of the lesion. Attempts to transmit the disease by inoculation of tissue suspensions and fluid from the lesions to experimental animals have been unsuccessful. Veterinarians have been unable to transmit the disease to cows and calves.

The Usefulness of Corticotropin and Corticoids in Patients with Liver Disease. M. A. Spellberg. Am. J. Gastroenterol. 26:342-353 (Sept.) 1956 [New York].

Corticotropin (ACTH), cortisone, and hydrocortisone were used as therapeutic agents in 10 patients with various diseases of the liver. In a 27-year-old man with infectious hepatitis, intravenous administration of 20 units of corticotropin daily was started at the end of the fourth week of his illness when the serum bilirubin level was 40 mg. per 100 cc. There was a nearly 50% drop of the serum bilirubin level within one week. Treatment with the same dose of the hormone was continued for two weeks and then gradually discontinued. The icterus disappeared in about four weeks, and the patient made an uneventful recovery. A 17-year-old boy with posthepatitic cholangiolitic cirrhosis started receiving 50 mg. of cortisone intramuscularly twice daily when his serum bilirubin level had increased to 24 mg. per 100 cc. after a temporary drop to 16.8 mg. per 100 cc. resulting from absolute bed rest and intravenous administration of dextrose and vitamins. The serum bilirubin level dropped again to 8.4 mg. per 100 cc. in two weeks. There was marked improvement of appetite and weight gain. After three weeks of treatment with cortisone, 40 units of corticotropin gel was given intramuscularly as a substitute for cortisone. This dose was gradually reduced and then withdrawn, but the serum bilirubin level rose again to 21 mg. per 100 cc. The jaundice could practically be titrated with the steroids. Steroid therapy had to be continued for about 18 months, after which time the liver was apparently able to function without assistance. No fatty liver developed in this patient.

Only one of six patients with hepatic coma (three with posthepatitic cirrhosis and one each with chronic, subacute, and acute hepatitis) who were given corticotropin and corticoids, survived and is still alive eight months after her first attack of coma. This was a 25-year-old woman who had had infectious hepatitis about six years previous to her admission to hospital for hepatosplenomegaly and jaundice in the fifth month of pregnancy. She delivered a premature but viable infant and three days later went into hepatic coma. She was out of coma after 72 hours of intravenous administration of 100 units of corticotropin daily. Two weeks after the treatment was changed to intramuscular administration of 40 units of corticotropin daily, she again went into hepatic coma. Administration of 100 units of corticotropin intravenously resulted in the patient's return to the precoma state within 48 hours. The patient was discharged four weeks after the last episode of coma on 40 units of corticotropin given intramuscularly. The postpartum hepatic coma may have been caused by a spontaneous reduction of endogenous adrenal steroids at the termination of pregnancy, and it was necessary to stimulate her adrenal glands more vigorously with large amounts of corticotropin. A 48-year-old man had a cholecystectomy and common duct exploration and drainage one year before jaundice recurred. There was a prompt drop of the patient's serum bilirubin level on administration of 100 mg. of cortisone intramuscularly. The patient was subsequently operated on again, and a carcinoma of the pancreas was found. This case shows that even in carcinoma of the pancreas the jaundice may be caused by an associated pancreatitis that responds to the anti-inflammatory influence of steroids. The last patient, a 57-year-old woman, who six years before had had a cholecystectomy for cholelithiasis, underwent an exploratory laparotomy because of epigastric pain, nausea, vomiting, pruritus, and jaundice. Liver biopsy showed an intrahepatic cholangitis. Pain and jaundice continued postoperatively. She was placed on therapy with 60 units of corticotropin gel, and the jaundice disappeared rapidly and completely.

Corticotropin and corticoids are useful therapeutic agents in protracted hepatitis with jaundice, fulminating hepatitis, hepatic coma, posthepatitic cholangiolitic cirrhosis, and perhaps other types of biliary cirrhosis. Steroid therapy may be of limited value in certain phases of portal cirrhosis, and it may have some limited value as a therapeutic test in differentiating between "medical" and "surgical" jaundice.

Lupus Vulgaris After BCG Vaccination. G. Høvding and P. Wetteland. Nord. med. 56:948-950 (July 5) 1956 (In Norwegian) [Stockholm, Sweden].

A case of lupus vulgaris at the site of BCG vaccination in a 46-year-old woman is described. The patient was Pirquet negative before the vaccination and had lived in a nontuberculous milieu for years. One week after inoculation in the shoulder by the multiple puncture method in January, 1950, local itching and exudation set in, with a slowly spreading lesion and peripheral superficial ulceration. When the patient was seen in December, 1951, the clinical picture agreed fully with lupus vulgaris and the histological picture revealed typical tuberculoid inflammation of the affected skin and regional lymph nodes. Tubercle bacilli were not demonstrable in cultures or on animal inoculation. The preceding BCG inoculation is believed to have been the etiological factor. The patient responded well to treatment with streptomycin, isoniazid, and PAS.

Effect of Intravenously Administered Solution of Honey on Dynamics of Circulation. K. Gotsch, E. Borkenstein and H. Clodi. Wien. Klin. Wchnschr. 68:647-651 (Aug. 17) 1956 (In German) [Vienna, Austria].

The effects of the intravenous administration of two preparations of solutions of honey on the dynamics of circulation were studied in six persons between the ages of 16 and 42 years with normal circulation. Three persons received intravenous injections of a 20% deproteinized solution of honey (Mel-P), which contained 812 mg. of dextrose, 834 mg. of fructose, and 343 mg. of saccharose and melezitose. After splitting by invertin the organism has at its disposal 878 mg. of dextrose and 1,129 mg. of fructose, i. e., a total amount of 2,007 mg. of sugar. The other three persons received intravenous injections of a preparation (Mel-S), which contained 20 mg. of vitamin B_1 and 0.125 mg. of strophantin in addition to the deproteinized solution of honey. Blood pressure, pulse rate, cardiac output, minute volume, elastic and peripheral total circulatory resistance, and cardiac performance were determined simultaneously with the consumption of oxygen. Recordings were made under conditions of basal metabolism.

The minute volume was somewhat reduced after the intravenous injection of the Mel-P preparation. The pulse rate did not show any significant change, and the reduction of the minute volume, therefore, was the result of a reduction of the cardiac output. Elastic and peripheral total circulatory resistance were not changed significantly. The blood pressure remained constant. These findings suggest a reduced energy stress on the myocardium. Observations on the persons receiving the Mel-S preparation showed that this circulation-sparing effect may be still further increased by the addition of strophantin to the honey. Simultaneous determinations of oxygen consumption showed that in some persons honey alone may cause a reduction of the consumption of oxygen in addition to a reduced energy stress on the myocardium. The acetylcholine content of the honey is considered responsible for the reduction in oxygen consumption, but this reduction also depends on the autonomous constitution of the person. The lowering of the cardiac performance by a reduced minute volume and the unchanged peripheral oxygen supply with improved oxygen utilization that characterize the change in the dynamics of the circulation after the administration of the honey-strophantin-vitamin B_1-mixture justify a therapeutic trial of this preparation.

Sternal Puncture: Its Indications and Limitations. B. M. Hurt and T. I. Robertson. M. J. Australia. 2:130-135 (July 28) 1956 [Sydney, Australia].

Studies were carried out to determine the part played by sternal puncture in the diagnosis and management of an unselected series of 272 patients in whom marrow was aspirated at a Sydney hospital during the years from 1945 to 1952. Thus there was adequate time for follow-up studies. The complete records and the progress of all these patients were studied, firm diagnoses were established, and the series was divided into three main groups and each of these into subgroups. There were 102 patients with anemias and related disorders, 85 with leukemias and reticuloses, and 85 with miscellaneous conditions including among others malignant disease, hepatic cirrhosis, chronic renal disease, bone disease, lymphadenopathies, abdominal tuberculosis, leprosy, and malaria. The diagnoses were made on the basis of the history, physical signs, laboratory investigations, and the progress of the disease. Reports on the pathology of excised nodes were available for many patients with lymphadenopathy. Autopsy was performed on 71 subjects, but, as many of the other patients are still living, the reaching of a diagnosis involved personal interpretation of clinical findings and is therefore subject to error. Doubtful cases were discarded from the series. In each instance the myelogram and the peripheral blood examination, made close to the time of the marrow puncture, were studied together.

Approximately 1 cc. of marrow fluid was aspirated and expelled directly onto slides, and thin films were spread. These were stained by the Jenner-Giemsa method and 500 cells were classified and counted. Other stains, such as peroxidase and Ziehl-Neelsen, were sometimes used. Bacteriological and cultural examinations were occasionally performed. Marrow samples were sometimes allowed to clot and were subsequently fixed, and sections were prepared to allow the general architecture and cellularity of the marrow to be studied; however, when this point was seriously under consideration trephine biopsy was employed. Information of greatest positive diagnostic value was obtained in patients with untreated pernicious anemia, multiple myeloma, the leukemias, and myelosclerosis, while confirmation of the diagnosis of hemolytic anemia and iron deficiency anemia was also provided. Sternal puncture was useful in excluding leukemia, multiple myeloma, myelosclerosis, and the diseases of lipoid storage when the blood count, physical signs, or results of other investigations indicated the presence of these diseases. Sternal puncture was useful in assessing the prognosis in patients with depression of the bone-marrow function, especially when neutropenia predominated. This investigation also revealed that examination of the marrow is of less importance than careful examination of the peripheral blood, and the marrow is usually found to be normal if the blood count is completely normal. Lymph-node biopsy is more informative than marrow biopsy in patients with both lymphadenopathy and a normal blood count. Nevertheless, although sternal puncture is rarely a short-cut to diagnosis, when it is properly used, confirmatory patterns and helpful negative results are often obtained.

Antidiuresis and Other Renal Responses to Piperoxan in Pheochromocytoma. A. C. Corcoran, H. P. Dustan and I. H. Page. Circulation 14:221-226 (Aug.) 1956 [New York].

Intravenous injections of 20 mg. of piperoxan hydrochloride were given to four patients with essential hypertension, to one patient with hypertension caused by acute glomerulonephritis, to four patients with functioning pheochromocytoma, and to one patient who had become normotensive after surgical removal of a pheochromocytoma. Piperoxan had a moderate renal vasodilatory effect and decreased the urine flow to about one-third of the pretreatment rate in the four patients with functioning pheochromocytoma. In contrast, it elicited slight renal vasoconstriction and usually increased the urine flow in the five patients with hypertension from causes other than pheochromocytoma and in the patient who had become normotensive after removal of a pheochromocytoma.

The antidiuretic effect of piperoxan in patients with functioning pheochromocytoma probably reflects inhibition of the renal vascular and tubular actions of norepinephrine and epinephrine and, insofar as it may correspond to the antidiuresis elicited by withdrawal of infusions of epinephrine and norepinephrine, may also involve posthypophyseal antidiuretic action. The diuretic effect of piperoxan in patients without pheochromocytoma is probably the result of a similar complex response. Since the antidiuretic effect of piperoxan in patients with pheochromocytoma has been larger proportionately than its effect on blood pressure, measurement of urine flow under standardized conditions is suggested as a simple, confirmatory guide in the diagnosis of pheochromocytoma.

Hepatitis and Diabetes. O. Günther. Ztschr. ges. inn. Med. 11:656-660 (July 15) 1956 (In German) [Leipzig, Germany].

Two factors deserve consideration in the explanation of the fact that jaundice due to hepatitis occurs more frequently in patients with diabetes mellitus than in persons without this disorder. First, patients with diabetes mellitus are more exposed to hematogenous infection because of the many blood sample withdrawals made even in diabetic patients who do not receive insulin injections. Furthermore, these patients are frequently hospitalized and during this time may receive one or several injections of insulin every day. (Daily insulin injections involve no danger if the patient uses his own equipment at home.) Second, there is the possibility that diabetic patients have a greater predisposition to infection in general and that their livers may be particularly susceptible to infection. The author investigated these factors on the basis of a statistical analysis of the records of 10,000 diabetic patients who were treated in diabetic departments between 1930 and 1954. This group included 755 patients (7.6%) who in the course of diabetes had one or several attacks of hepatitis. The incidence of hepatitis was highest during the first year after the diabetes became manifest. Furthermore, 693 (91.7%) of the 755 diabetic patients who contracted hepatitis received insulin injections, whereas the percentage of those requiring insulin injections was only 78.3% of the total. The author feels that these two facts show that diabetic patients are more likely to become infected with the virus of hepatitis by the hematogenous route. In view of the extreme heat resistance of the virus of hepatitis, more thorough sterilization of the injection instrumentarium was adopted at the author's clinic. Boiling the instruments used for insulin injection and for blood withdrawal for 20 minutes is regarded as inadequate, and hot-air sterilization at 160 C for 60 minutes or sterilization in the autoclave is demanded.

SURGERY

Structural Changes in the Heart Resulting from Cardiac Massage. G. H. Peddie, O. Creech Jr. and B. Halpert. Surgery 40:481-487 (Sept.) 1956 [St. Louis].

This report is concerned with the structural changes in the hearts of 14 patients on whom cardiac massage was performed and who subsequently died. Seven of the 14 patients died immediately of the cardiac arrest, one died at the end of six hours, and the remaining 6 died between 10 and 79 days later. Of these six patients, three died of cardiac arrest, while three regained consciousness but died later of their primary disease. Massage had been continued for up to 15 minutes in 10 of the patients, whereas in the remaining four it had been carried out for from one to five hours. The hearts removed at autopsy were fixed in formalin and were subsequently examined grossly and microscopically. As regards the immediate changes caused by cardiac massage, there was a traumatic, hemorrhagic pericardial effusion in the seven patients who died immediately and in the one who died after six hours. Other reports and the experience of these authors indicate that the effusion persists for at least 10 days and is followed by an outpouring of inflammatory cells and fibrin, so that the pericardial fluid becomes turbid with organization and fine fibrous adhesions. This reaction may progress to adhesive pericarditis.

There was evidence that the myocardial damage is in direct proportion to the duration of massage and is aggravated by previous myocardial changes. Epicardial hemorrhage and extravasations of erythrocytes between the myocardial fibers occur as a result of prolonged or too vigorous massage. Cardiac rupture may ensue if the traumatic myocardial changes occur in a heart already damaged by ischemia. This occurred in one of the 14 patients. There was evidence of some damage to the myocardium and pericardium in all the patients in whom massage lasted more than 15 minutes. Pericardial reaction, which was noted in nine patients, seemed to develop irrespective of the duration of massage and was not confined to patients whose pericardium had been opened. It is likely that manipulation of the heart and intracardiac injection of various agents are sufficient to produce pericarditis. No conclusions can be drawn from the use of the defibrillator in regard to cardiac damage, for in four of the five cases in which it was used there was also prolonged massage and the changes are attributed to this factor. Since cardiac massage is usually initiated hurriedly, manipulation tends to be vigorous, and when massage is continued beyond 15 minutes serious injury may follow. Experimental studies indicate that if performed carefully even prolonged cardiac massage will not damage the heart.

Causes of Death in One Thousand Operations for Congenital Heart Disease. W. J. Potts, W. O. McQuiston and T. G. Baffes. A. M. A. Arch. Surg. 73:508-516 (Sept.) 1956 [Chicago].

This report deals with operative and hospital deaths that occurred in 1,000 operations for congenital heart disease performed up to February, 1955, at the Children's Memorial Hospital in Chicago. The ages of the children ranged from 8 days to 16 years. There were 90 deaths and 89 postmortem examinations. The chief aim of the study was to learn which deaths were preventable. The postmortem examinations were often disappointing in that it was impossible to say which particular pathological change was the cause of death. In the group with cyanosis due to pulmonary stenosis remediable by surgery, the mortality year after year has remained near 9%. In the noncyanotic group the mortality has varied from zero in 347 operations for patent ductus arteriosus to 24% in patients with constricting vascular rings. The causes of death include errors due to oversight, poor judgment, and inexperience as well as to irremediable pathological conditions.

Patent Ductus Arteriosus in the Adult. H. Eliasch, K. Eriksson and L. Werkö. Acta med. scandinav. 155:135-156 (No. 2) 1956 (In English) [Stockholm, Sweden].

Thirteen women and four men between the ages of 18 and 47 years with patent ductus arteriosus were studied in an attempt to determine whether adult patients with patent ductus who are asymptomatic and those who have an excessive degree of pulmonary hypertension should be operated on. Eleven of the patients had normal pulmonary arterial pressure associated with high pulmonary blood flow; they were essentially free of symptoms. The remaining six patients had varying degrees of increased pulmonary arterial pressure and were more or less incapacitated. There was no correlation between age and pulmonary arterial pressure level. The oldest patient had normal pulmonary arterial pressure. Age also did not correlate with the size of the heart or the level of renal blood flow. On effort, pulmonary arterial pressure did not change in those patients who had normal pulmonary pressure when at rest. In patients with pulmonary hypertension, exercise generally caused a further rise in pulmonary arterial pressure. The systemic blood flow increased on effort in all patients. Whether this was caused by a reduced shunt or by an increase in the left ventricular output could not be assessed because of the difficulty of determining the pulmonary blood flow accurately. In patients with normal pulmonary pressure the renal blood flow was either normal or slightly reduced; in patients with pulmonary hypertension the renal blood flow was significantly decreased.

Five of the 11 patients with normal pulmonary arterial pressure were operated on. Surgical intervention and the immediate postoperative course were uneventful in four, but technical difficulty caused by a short and wide ductus was encountered in the course of the operation in one patient. The characteristic continuous murmur disappeared after the operation in all five patients, but it reappeared three weeks after the operation in the one whose operation was difficult. Follow-up catheterization revealed reopening of the ductus in this patient. All six patients with pulmonary hypertension were operated on. The operation and the immediate postoperative course were uneventful only in the oldest patient (aged 41 years) of this group in whom the pulmonary arterial pressure was restored to a normal level. One patient died during the surgical intervention from rupture of the pulmonary artery. Of the remaining four patients, one had failure of the right side of the heart and increased peripheral cyanosis three months after the operation; one had paraplegia, although the ductus was well closed and the size of the heart was markedly decreased after the operation; one patient was discharged with residual symptoms from arterial embolism; and one patient had a reactivation of rheumatic endomyocarditis but eventually recovered.

The importance of differentiating between so-called secondary and primary pulmonary hypertension in patients with preoperatively increased pulmonary arterial pressure is stressed. Two of the six patients with preoperatively increased pulmonary arterial pressure who had excessively increased pulmonary arterial pressure, normal pulmonary capillary venous pressure, and low pulmonary blood flow were therapeutic failures. The operative results were satisfactory in the other four patients with moderately increased preoperative pulmonary pressures, associated with increased pulmonary capillary venous pressure in two and with a low pulmonary capillary venous pressure and a high pulmonary blood flow in the two others. These four patients had so-called secondary pulmonary hypertension, and in patients of this type surgical intervention is indicated. Increased pulmonary blood flow alone is not responsible for the development of pulmonary hypertension. Anatomic narrowing and increased vascular tone in the peripheral pulmonary vessels may also be considered contributing factors.

omplete Anatomical Correction of the Tetralogy of Fallot Dects: Report of a Successful Surgical Case. C. W. Lillehei, M. Cohen, H. E. Warden and R. L. Varco. A. M. A. Arch. Surg. 73:526-531 (Sept.) 1956 [Chicago].

The authors report observations on a 17-month-old boy who was seriously ill with the tetralogy of Fallot defects and in whom complete anatomic restoration has been achieved. This is affirmed by his subsequent dramatic clinical improvement as well as by objective roentgenographic and catheterization studies carried out six months postoperatively. The technique of controlled cross circulation was utilized for the total bypass of the heart and lungs during the necessary interval of open cardiotomy. At that time the patient's ventricular septal defect was closed by the precise placement of silk stitches under direct vision. Next, the obstructing infundibular muscle was resected until an adequate outflow channel had been created. The boy's father served as the donor for the cross circulation.

Since March 26, 1954, the technique of controlled cross circulation for the total bypass of the heart and lungs has been used for reparative surgery under direct vision in 45 consecutive patients with a variety of cardiac lesions. From the knowledge and experience gained in these 45 direct-vision intracardiac operations with use of the cross circulation method, it has been possible to develop a simple, disposable, inexpensive, artificial oxygenator to replace the human donor, without sacrifice of the safety and effectiveness inherent in the donor method. Since then, with the use of this oxygenator and the same pump used for the cross circulation operations, 44 patients ranging in age from 4 months to 21 years have had their hearts and lungs totally bypassed for intervals of up to 50 minutes during direct-vision intracardiac correction of their defects. The patient reported is unique in that he is the initial patient to have the tetralogy of Fallot defects corrected with objective postoperative studies to corroborate his normal clinical appearance. Upon the basis of successes, as well as from the instructive failures, the authors have adopted the curative operation as the method of choice for all patients with the tetralogy of Fallot defects who are in need of surgical help at this time. For urgently ill patients in clinics where the curative operation may not be available as yet, the anastomotic operation without opening the pericardium is recommended only if they cannot be tided over by nonoperative management until the completely corrective operation becomes available to them.

Postoperative Wound Infection. R. A. Shooter, G. W. Taylor, G. Ellis and Sir James Paterson Ross. Surg. Gynec. & Obst. 103:257-262 (Sept.) 1956 [Chicago].

A rise in the incidence of infection in operative wounds at St. Bartholomew's Hospital in London led to an inquiry into its cause. The clinical facts suggested that infection was occurring in the operating room. A breach in surgical technique was not detected and it seemed that air-borne bacteria were responsible for the high infection rate of clean surgical wounds. Samples of the operating room air showed an abnormally high content of bacteria, and smoke testing of the ventilation showed that contaminated air from the surgical wards was being sucked into the room around the closed doors. The ventilation was modified so that the powerful input stream of pure air was directed across the operating table and out round the doors. This alteration greatly reduced the bacterial content of the air in the operating room, and the wound infection rate fell from 9 to 1%. The improvement was thought to be due to positive pressure ventilation of the operating theater and to avoidance of zones of still air over the operating table.

The Effect of Lowered Body Temperature on the Cerebral Hemodynamics and Metabolism of Man. H. H. Stone, C. Donnelly and A. S. Frobese. Surg. Gynec. & Obst. 103:313-317 (Sept.) 1956 [Chicago].

Studies performed upon animals indicate that hypothermia permits far longer periods of total cerebral vascular occlusion without sequelae than would be possible at normothermic levels. Since, however, the cerebral integration of animals is far less complex than that of man, Stone and associates studied the response of the human brain to acute reduction in body temperature. Measurements of cerebral hemodynamics and metabolism during periods of reduced body temperature were made on three surgical patients for whom hypothermia was employed as an anesthetic adjunct. In the absence of shivering, cerebral oxygen consumption was sharply reduced at body temperatures of 83 to 85 F (28 to 29 C). Within this temperature range, cardiac arrhythmias were infrequent. The effect of shivering upon the human cerebral response to hypothermia became evident particularly in the third patient. In spite of a reduction in body temperature to 82.6 F, cerebral metabolism increased 105% above the control value in the presence of shivering. The increase in cerebral oxygen consumption occurred despite a decreasing cerebral blood flow. This pattern of cerebral response to hypothermia with shivering closely resembles that observed after the intravenous administration of l-epinephrine, perhaps suggesting the importance of this drug in the mediation of the shivering reflex. These results demonstrate the danger of assuming that a reduction in cerebral metabolism always follows a reduction in body temperature. Total circulatory interruption at hypothermic levels in the presence of shivering for longer than three minutes could be extremely hazardous.

The cerebral blood flow decreased in all patients at hypothermic levels. Without the use of controlled respiration, a respiratory acidosis developed in each patient at hypothermic levels. Cerebral vascular resistance increased in each of the three patients at reduced body temperatures in spite of a consistent rise in carbon dioxide tension. Hemoconcentration and generalized vasoconstriction in response to hypothermia may have caused this increase. From the results of the studies on the first patient, which demonstrated a reduction in cerebral oxygen requirements to one-fourth the amount needed at normal body temperature, it might be concluded that, at a temperature of 83 F, cerebral ischemia could be safely tolerated for a period three times as long as the conventional three-minute interval, or a nine-minute period. This conclusion has been verified clinically in the human being by Swan and Bailey and their associates, but at body temperatures below 83 F. Until more is known about the degree of depression of the cerebral metabolism of man at specific hypothermic levels, it cannot be assumed that all patients will respond in like manner.

Evaluation of Pelvic Exenteration for Advanced Cancer of the Cervix. A. Brunschwig and W. Daniel. Surg. Gynec. & Obst. 103:337-341 (Sept.) 1956 [Chicago].

Since September, 1947, pelvic exenterations have been performed at Dr. Brunschwig's service in 441 patients with various forms of advanced pelvic cancer. This report is concerned with the 336 patients with carcinoma of the cervix in whom either complete or anterior pelvic exenteration was performed. Ninety-three or 27% of the patients had new cases, most of them being in either stage 3 or 4 (League of Nations classification). In the past two or three years more anterior exenterations have been performed in stage 2 cases in the presence of actual parametrial involvement and encroachment on the bladder or ureter. Three groups of patients had undergone definitive surgery with or without irradiation. One group had been treated by surgery alone, another had been subjected to conservative surgery after an attempted cure by irradiation, and in the third group conservative surgery had been followed by irradiation for recurrence. The decision to resort to exenteration was based on the extent of disease present and not on the type of previous treatment. In the earlier phases of this program, patients were not infrequently operated on for palliative purposes only. In these instances, diseased tissue was sometimes left behind. The results were poor. Now the tendency is not to attempt exenteration unless previous exploration at laparotomy indicates that all macroscopic evidence of disease can be removed.

Of 55 surgical deaths, 19 were due to shock, 7 to peritonitis, 6 to sepsis, 6 to uremia, 5 to intestinal fistula, 2 to pulmonary embolism, 2 to cerebral accident, and others to late hemorrhage, pneumonia, hepatitis, gastrointestinal obstruction, or unknown causes. Exenterations were initially undertaken for palliation only. No "cures" were expected at first. Palliation continues to be an objective, inasmuch as a 22.4% three-year survival rate was achieved. That a five-year survival can be offered is attested to by its 15% incidence in 111 minimally selected patients. Exenteration benefits patients with advanced pelvic cancer, especially those with recurrences after failure of radiation or more conservative forms of surgery.

Factors Influencing the Spread of Cancer. G. Crile Jr. Surg. Gynec. & Obst. 103:342-352 (Sept.) 1956 [Chicago].

The importance of the passage of time in the spread of cancer receives different emphasis in the two popular theories on the subject. The most widely supported theory is the concept that cancer starts as a localized disease, spreads to the regional lymph nodes, and with further passage of time spreads throughout the body. The second is the theory called by Ian MacDonald "biologic predeterminism," which holds that each cancer has certain biological characteristics that tend to remain more or less constant throughout its life. In this concept it is the type of tumor and the resistance of the host that largely determine the spread of cancer. Crile believes that it is impossible to prove or disprove that either of these concepts affords a complete explanation of the spread of cancer. In some cancers, such as those of the skin, the factor of time is not so important as is the type of the cancer and its biological behavior. A basal cell cancer of the skin rarely metastasizes to lymph nodes regardless of how long it is left untreated; a squamous cell cancer of the skin usually metastasizes only to lymph nodes and rarely metastasizes systemically; and, finally, a melanoma may metastasize systemically even before the primary tumor is noticeable. Cancers of the thyroid, like cancers of the skin, can also be separated into biological types. We know much less about cancers of the internal organs, and so it is easy to assume that it is the passage of time that causes a localized disease to become systemic. It is easy to assume that a localized cancer of the stomach is a young cancer that has not been present long enough to spread and that a diffusely metastasizing cancer is an old cancer that has been present long enough to allow it to metastasize. Yet in individual cases we know that primary cancers of the stomach that have given rise to systemic metastases may be so small that they are not recognizable on gross examination and that large cancers of the stomach, known to be present for several years, are often localized.

The author comments on the failure of early and radical treatment to alter the death rate from cancer, on the causes of this failure, and on the danger of the dissemination of cancer and the importance of the lymph-node barrier. Some types of localized cancer are well adapted to radical surgical attack. When cancers of the gastrointestinal tract are causing obstruction, infection, pain, or hemorrhage, prompt operation is mandatory and often lifesaving. Radical resection of pelvic organs for localized central recurrences of cancer of the cervix may eliminate all residual cancer, and, if the ureters are properly transplanted, the patient may enjoy a comfortable and useful life. But perhaps other cancers, such as infiltrating "leather-bottle" cancers of the stomach, when they are causing minimal symptoms and by their very type are not curable by resection, should be viewed in the same light as inflammatory cancers of the breast and operation should be avoided. A therapeutic trial of roentgen therapy to rule out lymphosarcoma might be preferable to the risk of dissemination that is incurred by exploration and biopsy. A policy of watching the development of this type of cancer and doing nothing so long as the symptoms are not severe might result in increased comfort and length of life. Perhaps in older people thorough electrocoagulation of selected low-lying cancers of the rectum may be perferable to combined abdominoperineal resections. Better results might be obtained if each cancer and each patient with cancer were dealt with as an individual problem. The author admits that these thoughts about cancer are not answers to the problems of its treatment but merely raise questions that should be considered before we generalize too much about cancer and place too much reliance on the classic philosophies and techniques. The greatest challenge is to recognize patients whose cancers are adapted to surgical cure and to avoid operating on those in whom intervention does nothing but harm.

The Etiology and Prevention of Volkmann's Ischemic Contracture. P. R. Lipscomb. Surg. Gynec. & Obst. 103:353-361 (Sept.) 1956 [Chicago].

The records in 92 cases of Volkmann's ischemic contracture seen at the Mayo Clinic from 1935 through 1954 were reviewed. Forty-four of the contractures developed after supracondylar fractures of the humerus, and 18 followed fractures of both bones of the forearm. Other causes were fractures of the shaft of the humerus (7 cases), severance of a major artery or arteries as the result of lacerations or gunshot wounds (7 cases), dislocation of the elbow (4 cases), and miscellaneous conditions (12 cases). The miscellaneous group was of special interest. The contractures in three of these patients developed from fractures about the elbow itself; two patients had fractures of the shaft of the radius alone, and one patient sustained multiple fractures of the humerus, both bones of the forearm, and the hand. Two patients had crushing and contusing injuries without fractures. Another patient sustained a wringer injury in which the skin was not broken but a large hematoma appeared in the antecubital fossa. Another patient was a true hemophiliac who bruised his arm six weeks before he came to the clinic; bleeding continued, and it was necessary to amputate the arm below the elbow. Another patient had undergone operation for congenital synostosis of the radius and ulna four months before examination at the clinic; the extremity had been immobilized in a cast in extension. The last patient in the miscellaneous group had been operated on for a traumatic arteriovenous fistula at the level of the elbow four months before coming to the clinic.

The author believes that in the light of knowledge available in 1935, 38 of the 92 contractures were preventable and that, with present-day information, 61 of the contractures would probably be preventable. Observations on the 92 patients and on another group of 10 patients who were seen from 1 to 72 hours after injury and on whom arteriectomy was performed because of irreparable arterial damage and impending Volkmann's contracture in some lead to the following conclusions: 1. Arterial injury with associated vascular spasm is the most important cause of Volkmann's ischemic contracture. 2. Major arterial obstruction is not so important in the production of the contracture as is the associated spasm of the collateral blood vessels. 3. Early and adequate treatment of acute vascular spasm is necessary, even though it means surgical exploration of the antecubital fossa and forearm and resection of the injured or thrombotic segment of the brachial, radial, or ulnar artery. 4. In compound or other fractures and severe crushing and contusing injuries of the forearm accompanied by severe edema, attempts should not be made to close the wound primarily; instead, extension of the original wounds and the use of relaxing incisions are often indicated.

Resection in Pulmonary Tuberculosis: Results and Follow-Up of 700 Cases. J. J. Hirdes and C. I. Stegerhoek. Dis. Chest. 30:277-288 (Sept.) 1956 [Chicago].

Seven hundred patients with pulmonary tuberculosis underwent lung resection at a sanatorium in Bilthoven, Holland, between October, 1949, and February, 1954. Pneumonectomies were performed on 127 patients, lobectomies on 385, segmental resections on 187, and bilateral resection on one. There were 364 male and 336 female patients between the ages of less than 10 and up to 70 years, most of whom were between the ages of 20 and 30 years. The patients were followed up to Feb. 1, 1955. At this time, 23 patients had died, a mortality rate of 3.3%. Death resulted from the operation in 12, 4 died of various complications during their sojourn in the sanatorium after the operation, and 7 died after discharge. Of 584 patients aged less than 40, 14 (2.4%) died. Nine (7.2%) of 116 patients over 40 years of age died. The risk of lung resection increases with age.

Postoperative tuberculous empyema occurred in nine patients and micrococcic (staphylococcic) empyema in four. Ten of the 13 patients with empyema had a bronchopleural fistula. With good surgical technique and proper evaluation of indications, or with good preliminary treatment, this complication has become rare. The great danger of development of resistant tubercle bacilli should always be kept in mind whenever antibiotics are used. If resistance has developed, then lung resection will be a dangerous operation. Not one case of tuberculous empyema was observed among the last 400 patients operated on. Empyema occurred particularly after resection of the upper lobe together with the apical segment of the lower lobe. In such cases there is danger that the remaining lung tissue is insufficient to fill the thoracic space. A space filled with air or exudate may result, and this predisposes to tuberculous empyema. Only when the middle and lower lobes have become enlarged as the result of preoperative contraction of the upper lobe can resection of the upper lobe with the apical segment of the lower lobe be considered. If reexpansion within six or eight weeks after the operation is incomplete, a thoracoplasty from the second rib up to and including the fifth rib may be considered.

In a follow-up of from two to five years, relapses occurred in 50 patients (7%). On Feb. 1, 1955, 92% of the patients operated on were in good condition and well. The best results were obtained in patients operated on for restricted, well-localized lesions of low activity, such as primary foci, tuberculous caseous foci, and tuberculomas. Results were less satisfactory in those with active, far-advanced forms of tuberculosis with cavitation.

P-Hydroxypropiophenone for Advanced Breast Cancer: A Preliminary Report. B. A. Stoll. M. J. Australia 2:181-183 (Aug. 4) 1956 [Sydney, Australia].

Although estrogens and androgens have the power to inhibit the growth of breast carcinoma, both these hormones may have unpleasant side-effects—nausea, vomiting, and uterine bleeding in the case of the former and virilization and fluid retention in the case of the latter. A search is therefore proceeding for a material that will induce pituitary gonadotropic hormone inhibition without the undesirable estrogenic effects. Lacassagne, in 1940, succeeded in modifying the chemical structure of synthetic estrogens so that they lost their peripheral estrogenic action. The new compound PHPP or POPP represents one-half of the diethylstilbestrol molecule. Its estrogenic activity is 1/10,000 to 1/1,000 of that of estrone or stilbestrol. Experimental work with p-hydroxypropiophenone (POPP) appeared to be at variance until the level of dosage was clarified, and reports on clinical trials of the compound likewise seemed contradictory. This report is concerned with 13 patients with advanced breast carcinoma, who were treated with POPP at a dose of from 1 to 10 gm. per day (0.02 to 0.2 gm. per 1 kilogram of body weight). Three levels of dosage were chosen, i.e., 1 gm., 5 gm., and 10 gm. per day. Only five of the patients were given 5 gm. or more per day, and only three of them received this dose for two months or more. Estrogens generally require six or eight weeks to become effective. Two of the three patients showed almost complete regression of nodular recurrences of breast carcinoma, and the third showed no change. No beneficial effects were obtained at doses of 1 gm. per day.

This is a preliminary report, as the number of cases is small. However, the principle involved is a most important one. The use of a pituitary-inhibiting compound without peripheral estrogenizing effect would have a wide field in the treatment of advanced breast carcinoma. Many patients complain of the nausea, vomiting, and uterine bleeding associated with estrogen administration in high dosage; more important, however, is the younger patient, to whom estrogens may not be given on account of the danger of exacerbation of the disease. The only hormone available for this group is testosterone, and the use of POPP avoids the virilization that ensues from the use of the male hormone.

Carcinoid Tumors of the Stomach. R. Lattes and C. Grossi. Cancer 9:698-711 (July-Aug.) 1956 [Philadelphia].

The authors described pathological findings in carcinoid tumors of the stomach in four men and one woman between the ages of 28 and 74 who underwent local excision or gastric resection at the surgical department of the Columbia-Presbyterian Medical Center in New York. Thirty-five additional cases were collected from the literature. The most interesting biological and clinical feature of these tumors is that, whenever surgical resection is possible, long-term clinical arrests can be expected, even in the presence of regional metastases. One of the five patients was alive and well 13 years after the discovery of retroperitoneal metastases and 12 years after resection of the primary tumor; one was living and well 13 years after subtotal gastrectomy and demonstration of metastases in the regional lymph nodes; and one was living and well 9 years after local excision. In the fourth patient, the carcinoid tumor was an incidental microscopic finding in a stomach resected for extensive carcinoma of the midgastric portion. The fifth patient had a large, fungating carcinoid tumor with regional lymph-node metastases for which he was operated on too recently to make evaluation possible. The gross and microscopic features of the tumor were notable. Grossly it resembled closely the common fungating adenocarcinoma. Microscopically, it was unusual in that, along with the classic histological structure of a carcinoid tumor, there were groups of mucus-secreting neoplastic glands The possible occurrence of glandular lumina in otherwise typical carcinoid tumors has been recognized by other workers and should be accepted as an occasional histological variant of these tumors. Three of the five patients had definite hyperchromic anemia.

The unique biological behavior of these tumors, with slow progression even after regional metastases have occurred, makes them a clinical as well as a pathological entity. In the evaluation of long-term results after surgery for gastic cancers, these neoplasms should always be segregated from the larger and more malignant group of the other metastasizing epithelial tumors of the stomach.

Spontaneous Passage of Necrotic Bowel. W. M. Cavies and J. D. Hicks. Australian & New Zealand J. Surg. 26:66-69 (Aug.) 1956 [Melbourne, Australia].

The patient was a 59-year-old woman on whom a cholecystectomy was performed. Seventeen days after the operation she passed 18 inches of necrotic colon after attacks of abdominal pain and diarrhea. At an operation a month later it appeared that the descending colon became necrotic and was sealed off by adhesions. To counteract this blockage a fistula between the sigmoid and the ileum had fortunately developed, allowing the excretion of intestinal contents. In spite of the breakdown of the upper abdominal wound as the result of the underlying hematoma, healing occurred and the patient went home with a colostomy after three months. At a third operation the descending colon was found to be reduced to a dense fibrous cord. In spite of dense adhesions, both in the splenic flexure and in the pelvis, the colon was reconstituted. Although the spontaneous separation of a segment of necrotic colon is rare, it has been observed before. The necrosis of the descending colon was probably due to thrombosis of the vascular supply, of the left colic artery for instance, rather than to an intussusception, the lack of a mesentery restricting any infolding of the colon. The retroperitoneal situation of the affected portion was probably responsible for the prevention of widespread peritonitis. As the damage extended into the sigmoid colon, an ileosigmoid fistula resulted. This fortuitous complication allowed the passage of intestinal contents, possibly more fluid than usual by virtue of the short-circuiting of the major portion of the colon. The closure of this fistula necessitated a transverse colostomy. The localized hematoma in the upper abdomen and the inflammatory collection in the pelvis were potent factors in delaying healing but the patient recovered steadily.

Major Vascular Injuries Incident to Intervertebral Disk Surgery. J. R. Mack. Am. Surgeon 22:752-763 (Aug.) 1956 [Baltimore].

Mack presents the histories of four patients in whom damage to the major vessels occurred in the course of intervertebral disk surgery. These four patients, treated by different teams in four different hospitals in the Cincinnati area, demonstrate a number of interesting points. The one patient in whom the surgeon was aware of the danger of this complication and recognized its occurrence was promptly and successfully treated by ligation of the left common iliac artery. Of the three patients in whom the operator was not aware of this danger and the injury was not recognized, two died of massive hemorrhage and one rapidly developed a large and disabling arteriovenous fistula. Observations on these patients and a review of the literature show that injury to the major vessels is an ever-present hazard during surgical interventions on intervertebral disks and can occur in the hands of the most competent and careful surgeons. The prone position of the patient on the operating table, with anteflexion of the spine, compresses the major vessels against the spine, thus putting them in an extremely vulnerable position and masking the injury when it does occur. The pituitary forceps is the instrument most commonly responsible for vascular damage. Awareness of the danger, although extremely important, is no assurance that the injury will not occur. The ease with which bleeding is controlled by means of Gelfoam or Oxycel is not a safe criterion as to the extent of the injury. It is usually not manifested by excessive bleeding, and so it must be recognized by careful postoperative observation.

Prompt recognition and treatment is the only method of reducing the disastrous mortality rate. The method of treatment may vary according to the site and extent of injury. Restoration of the continuity of the injured vessels by suture or arterial graft may at times be desirable but is by no means always essential; ligation alone may in some instances be simpler and safer. The common iliac artery, which is the most frequent site of injury, can be ligated with relative impunity because of its extensive collateral circulation. An arteriovenous aneurysm involving the common iliac artery can be treated by ligation of the artery above and below the fistula, leaving the small segment of artery attached to the vein because of the absence of branches in this portion of the artery. Immediate sympathectomy has been advocated, but is not essential for preservation of the viability of the extremity.

NEUROLOGY & PSYCHIATRY

Prevention of Paralysis in Poliomyelitis by Rest. T. Brehme. München. med. Wchnschr. 98:1064-1065 (Aug. 10) 1956 (In German) [Munich, Germany].

Paralytic symptoms are more frequent and more severe in poliomyelitis patients who continued their usual activities during the prodromal symptoms than in those who kept strict bed rest from the onset of the symptoms. Muscular exertion was observed to have a localizing influence on the subsequent development of paralysis affecting muscles that were subjected to special exertion. The chemical processes that take place within the ganglion cell while it is functionally active and also when it is invaded by a virus show why rest is essential during poliomyelitis and why neuromuscular exertion may have harmful effects. Paralysis is both more frequent and more severe in large muscles than in the smaller ones. This fact suggests that, the more active the ganglion cell, the more rapidly the virus affects its cellular metabolism and the more harmful the effect of the virus on the cell. The inactive or quiescent cell has a better prospect of being protected against the virus.

The effect of physical rest in bed can be augmented by the use of "hibernation" drugs, such as phenothiazine derivatives, particularly megaphen. These drugs proved helpful even in patients with imminent or beginning respiratory insufficiency. The author induced therapeutic sleep lasting for from three to five days by a combination of phenothiazine derivatives in 36 children and adults with bulbar-pontine poliomyelitis. This helped the patients over the critical period, and in 28 of them the use of the iron lung could be dispensed with. The favorable effect of this treatment is ascribed to the elimination of disturbing influences from the cortex and hypothalamus. The rest induced by the phenothiazine derivatives is not a therapeutic but rather a preventive measure. Only when these preventive measures are applied early enough can the destruction in the ganglion cells be avoided.

Habit-Forming Properties of Meprobamate (Miltown or Equanil). F. Lemere. A. M. A. Arch. Neurol. & Psychiat. 76:205-206 (Aug.) 1956 [Chicago].

Because meprobamate has been advertised as being non-habit-forming, the author wishes to modify a preliminary report in which he stated that meprobamate was not habit-forming. Further clinical experience has convinced him that this drug is habit-forming in some patients. Withdrawal symptoms are sometimes experienced. Patients occasionally describe a feeling of "nervousness" and "jitters" above their premedication level of tension, or a feeling of "let down," when they miss their usual dose of meprobamate. Six patients who had formerly been addicted to alcohol and barbiturates stopped taking meprobamate because, as they said, they felt they were "getting hooked" or addicted to the drug and "wanted no part of it." One patient who had been taking large doses of meprobamate had a convulsion (the only one he had ever had) 10 hours after discontinuing this medication.

The author observed 13 patients, among more than 600 for whom he prescribed meprobamate, in whom the drug had to be withdrawn because of excessive self-medication. The patient, or more frequently the relatives, will call up and say the patient is acting exactly as if he were drinking. The danger of driving a car while under the influence of excessive meprobamate medication is self-evident. Of the 13 patients, 10 were alcoholics who were abstemious at the time. It is especially urgent to watch for excessive self-medication and abuse when meprobamate is prescribed for alcoholics. The author does not wish to depreciate the clinical value of meprobamate, which he still regards as the most helpful and least harmful of all the drugs used for the relief of nervous and emotional tension.

Atypical and Minor Epileptic Seizures. J. Moossy. J. Louisiana M. Soc. 108:331-336 (Sept.) 1956 [New Orleans].

Patients who complain of bizarre alterations of consciousness, which may be brief or prolonged but are less dramatic than a generalized epileptic seizure, pose different diagnostic problems. If the patient has grand mal seizures in addition to these minor atypical or partial episodes, the physician usually grasps the relationship. However, if a patient has only minor seizures, their epileptic nature may not be promptly appreciated. The term "epileptic equivalents" has been used in the past for such phenomena, although clinicians since Hughlings-Jackson have realized that these attacks are epileptic, just as the generalized convulsion is, and the term "equivalent" has no significance. The clinical manifestations are so polymorphous and the structures possibly involved so complex (temporal lobe, insula, rhinencephalon, diencephalon) that descriptive or anatomic terminology is too cumbersome for routine clinical use. Among clinicians particularly interested in the disorder, clinical, anatomic, and electroencephalographic observations are often utilized in nomenclature; however, for most clinicians, recognition of these seizures and their varied etiologies is enough, and the term, minor epileptic seizures, is probably adequate.

The histories of five patients are presented. They were selected from a routine office and hospital neurological practice. Patients with similar histories also visit general practitioners and specialists. If the physician thinks that a given patient with minor or atypical seizures has epilepsy, some thought should be given to distinguishing grand mal, petit mal, and Jacksonian types from the type of seizures under consideration. This can be done by clinical analysis of the seizure patterns. This also gives clues to the areas of brain involved. With tentative localization, various etiological factors should be considered in the light of the past medical history, age of onset, and the results of a complete study of the patient. In two of the five illustrative cases no obvious cause of the seizures could be determined. Of the other three patients, one had had measles encephalomyelitis, one a malignant brain tumor, and one an old head injury. Treatment depends on the cause. In patients with focal lesions, such as tumors or vascular malformations, palliative or curative neurosurgical therapy is of great importance.

PEDIATRICS

Fetal Hepatitis. W. Kiaer. Ugesk. læger 118:865-868 (July 26) 1956 (In Danish) [Copenhagen, Denmark].

Infants with fetal hepatitis who are stillborn or die perinatally as a rule present no clinical signs of hepatic affection. Histologically, they show extraordinarily marked hepatic changes, which may find remarkably weak macroscopic expression. In those who survive the first few days symptoms set in that strongly suggest occlusion icterus; only in rare cases does the condition fail to simulate occlusion icterus. Some cases depend on transplacental transmission from mothers with latent infection, but other noxae, particularly blood incompatibility, may cause the hepatic changes. To these two groups of children with fetal hepatitis a third group, consisting of children who between the ages of 2 and 10 develop symptoms of chronic liver disease, may perhaps be added. They may conceivably represent cases of the disease so mild that they did not produce symptoms at birth but gradually passed over into a chronic hepatitis or cirrhosis, as can be seen in adults with acute virus hepatitis.

Fetal Hepatitis with Perinatal Death in Four Siblings. W. Kiaer and M. Olesen. Ugesk. læger 118:868-872 (July 26) 1956 (In Danish) [Copenhagen, Denmark].

A clinically well woman had given birth to three living children. Six later pregnancies were followed by perinatal death. None of the infants showed signs of hepatic affection. Microscopic examination of the liver in four cases revealed characteristic grave fetal hepatitis. A chronic latent virus infection in the mother is suggested in possible explanation of the fetal hepatitis. Serologic and histological examinations testified against erythroblastosis and syphillis. Fetal hepatitis will probably rarely be diagnosed in infants who die shortly after birth, and only autopsy can give certain diagnosis. The cause of death in the other two siblings was not established.

Purpura in Childhood: Observations in 187 Cases. S. D. Mills. J. Pediat. 49:306-315 (Sept.) 1956 [St. Louis].

One hundred eighty-seven infants and children less than 15 years old, more than half being 6 years of age or less, who had purpura of different types, were observed at the Mayo Clinic between 1945 and 1955. The distribution of patients according to sex varied little with age or with type of purpura. This sex distribution is contrary to that in adults, among whom women significantly outnumber men. One hundred five of the 187 patients had thrombopenic purpura and 82 had nonthrombopenic purpura. This difference in number of cases does not indicate the probable relative frequency of the two types of purpura in children as it is observed in general practice but rather reflects the increased number of patients referred for study because of difficult problems of bleeding and because they might require splenectomy. In 27 of the 105 patients with thrombopenic purpura, the condition was secondary to infection and in 78 it was idiopathic, i. e., there was no evident cause for the bleeding, such as drug reactions, vitamin K deficiency, or an underlying blood dyscrasia such as leukemia or aplastic anemia. Forty-nine of the 82 patients with nonthrombopenic purpura had the so-called anaphylactoid or allergic type, which is believed to be the result of capillary damage caused by drugs or by allergens that are usually bacterial in nature and result from recent infection. Seventeen patients had bleeding into the skin in the course of or after an infection. Ten of the remaining 16 patients with nonthrombopenic purpura had a vascular defect, and the purpura was not caused by any discernible allergic mechanism; the purpura was factitial in 2, orthostatic in one, congenital in one, and caused by a drug in one. None of these patients had a lack of platelets or a demonstrable defect of clotting.

In general, the prognosis for all types of purpura in children is good. Eleven of the 187 patients died, and all of them had thrombopenic purpura. Four of these deaths were in the idiopathic thrombopenic group; three of the four patients had acute purpura, one with generalized and fulminating hemorrhage and two with sudden, fatal cerebral hemorrhage; the fourth, a 14-year-old girl, died of uncontrolled menorrhagia. In the secondary, either thrombopenic or nonthrombopenic, types of purpura, the underlying condition should be sought out and treated. Eighteen children with the thrombopenic type of purpura and nine with the nonthrombopenic type were treated with steroid hormones for the control of bleeding, but the results were disappointing. Splenectomy was performed on 54 of the 78 patients who had idiopathic thrombocytopenic purpura. Fifty of the patients reported on were followed up for from 1 to 10 years; 37 were well and 8 were improved. Thus 90% of the traced patients were benefited. Two patients died in the postoperative period. These two fatalities represent a mortality rate of 4%, which does not seem excessive in view of the severity and chronicity of the illness in many patients. The risk of intracranial bleeding and of the continuance of purpura into adult life or into the menstrual age in girls should be considered in the determination of the treatment to be used.

Studies of Tocopherol Deficiency in Infants and Children: II. Plasma Tocopherol and Erythrocyte Hemolysis in Hydrogen Peroxide. H. M. Nitowsky, M. Cornblath and H. H. Gordon. A. M. A. J. Dis. Child. 92:164-174 (Aug.) 1956 [Chicago].

Simultaneous determinations of plasma tocopherol levels and lysis of red blood cells in hydrogen peroxide were made in 73 women on the obstetric wards of the Sinai Hospital in Baltimore within the first 24 hours of the postpartum period, in 15 normal adults, in 122 full-term and 14 premature unfed newborn infants, in 55 full-term infants fed cow's milk mixtures and 14 fed breast milk, in 28 thriving premature infants fed partially skimmed cow's milk mixtures, and in 16 infants and children with steatorrhea associated with cystic fibrosis of the pancreas or biliary atresia. The effect of tocopherol supplementation was determined in premature infants and in the infants and children with steatorrhea. The mean plasma tocopherol levels in the normal adults (0.75 mg. per 100 cc.) and in the postpartum mothers (1.07 to 1.56 mg. per 100 cc.) were markedly higher than those of the newborn infants (0.22 to 0.26 mg. per 100 cc.). Breast feeding was associated with a rise in mean tocopherol level to 0.72 mg. per 100 cc., and feeding of cow's milk mixtures, with a smaller but statistically significant rise to a mean level of 0.33 mg. per 100 cc. in infants of the average age of 46 days. Prematurely born infants fed partially skimmed cow's milk showed a decrease in plasma tocopherol levels from 0.26 mg. per 100 cc. in the first 10 days to 0.13 mg. per 100 cc. in infants over 30 days of age. Oral supplementation with small doses of tocopherol esters led to prompt rises in plasma tocopherol levels. Infants and children with cystic fibrosis of the pancreas or biliary atresia showed low plasma tocopherol levels, the average of 42 observations being only 0.15 mg. per 100 cc. Oral supplementation of tocopherol esters led regularly to a rise in plasma tocopherol levels of patients with cystic fibrosis. In patients with biliary atresia intravenous administration was necessary to produce consistent rises.

The hydrogen peroxide hemolysis test is a convenient method for separating patients with plasma tocopherol levels below and above 0.5 mg. per 100 cc., except in unfed newborn infants. Analysis of simultaneous determinations of plasma tocopherol levels and hydrogen peroxide hemolysis indicated that when the tocopherol level was above 0.5 mg. per 100 cc. appreciable hemolysis was rarely present. When tocopherol concentration was below 0.5 mg. per 100 cc. a statistically significant inverse correlation was found in young full-term and premature infants fed cow's milk mixtures and in infants and children with steatorrhea. No correlation was found in unfed newborn infants, virtually all of whom showed low plasma tocopherol levels, suggesting that factors in addition to plasma tocopherol are important in determining susceptibility to hydrogen peroxide of the erythrocytes of newborn infants.

Treatment of Measles Encephalitis with Corticotropin. E. Appelbaum and C. Abler. A. M. A. J. Dis. Child. 92:147-151 (Aug.) 1956 [Chicago].

Corticotropin (ACTH) was given to 17 consecutive children between the ages of 1½ and 10½ years with measles encephalitis. Fourteen of the patients had convulsions and 10 were in a state of coma. The daily dose of the hormone varied from 5 to 80 mg., and the total amount of corticotropin given to individual patients ranged in most of them from 100 to 320 mg. In 11 patients, remission of the fever and a decisive improvement in the mental state were observed within from one to four days. In the remaining six patients these changes became evident within from 6 to 13 days. None of the patients died. Fourteen of the patients were discharged from the hospital without any neurological or other detectable abnormalities. Three patients showed, at the time of their discharge, residual central nervous system stigmas, including impairment of vision, loss of speech, euphoria, and mental retardation. Follow-up studies carried out for from seven months to three years and nine months in 16 patients revealed that 15 of these escaped without residual symptoms. In one patient there were marked neurological sequelae. While this series is too small to permit definite conclusions, nevertheless the favorable results obtained in all but one patient suggest that corticotropin has a beneficent effect in measles encephalitis. Corticotropin should be given a clinical trial in measles and other forms of demyelinating encephalomyelitis. It would seem advisable to administer the drug before the time when the degenerative change of demyelinazation is apt to appear, i. e., before the third day of the disease.

Rupture of Liver in Infant, with Survival. E. Soto Pradera, J. S. Latour, C. Granda Leon and A. Carbonell Salazar. Rev. cubana pediat. 28:439-442 (July) 1956 (In Spanish) [Havana, Cuba].

Rupture of the liver is rare in newborn infants and still rarer in older infants. The rupture may result from trauma in the region of the liver or from disruption of a subcapsular hematoma, which is formed during birth, passes unobserved for a few days or a few weeks, and then ruptures. Eight cases reported in the literature were in newborn infants. The patients survived after suture of the liver. Of infants 2 to 6 months old, only one survived after a suture of the liver. The case reported by the author is the second of this type. An infant 4½ months old was hospitalized because of sudden appearance of intense paleness. There was no history of trauma. The number of erythrocytes was low but increased after a transfusion of 100 cc. of whole blood. The patient refused feeding but did not vomit. The roentgen examination of the abdomen showed opacity of the intra-abdominal shadows (a sign that has been recognized in the literature as showing intra-abdominal hemorrhage.) A diagnosis of intra-abdominal hemorrhage (probably due to rupture of the liver) was made, and an operation was performed. A transfusion of 500 cc. was given in the course of the operation. The peritoneum appeared dark blue, and 500 cc. of blood and coagula was eliminated. After aspiration of the blood and cleansing of the operative field, a rupture 1 in. long was detected on the lower surface of the liver. This was sutured. The operation ended without complications. The postoperative period was complicated by high fever and vomiting. The treatment consisted of blood transfusions and intravenous administration of fluids, penicillin, streptomycin, sulfamide, cortisone, vitamin K, and thromboplastin. The patient was discharged from the hospital three weeks after the operation in excellent condition and with an increased body weight. She was normal three months after the operation.

DERMATOLOGY

Hemangioendothelioma. R. L. Cormie. A. M. A. Arch. Dermat. 74:144-148 (Aug.) 1956 [Chicago].

Cormie reports on a patient with hemangioendothelioma because of the extreme rarity of this condition. The patient was a 52-year-old woman who, when first seen in September, 1954, complained of pea-sized to hazelnut-sized lumps of one month's duration. The lumps were noticed first on the outer aspect of the right upper arm and then in the area of the right trapezius and in each breast. Many similar subcutaneous nodules appeared on limbs and trunk in subsequent weeks, especially on the abdominal wall. The first lesions were skin-colored, but many became bluish-red or red, and some became firmly adherent to the overlying skin. They were occasionally painful and were slightly tender to touch. The patient complained of progressive weakness, which necessitated her confinement to bed from Oct. 15. Thereafter her condition steadily deteriorated; she died on Dec. 15, 1954. Autopsy was refused. At a biopsy one nodule had been removed from the breast and one from the right arm. Grossly they appeared to be hemorrhagic areas of rather "meaty" appearance. Microscopic studies revealed lesions consisting of areas of short, plump spindle cells closely packed together with a rich reticular fibrillar stroma. In places, blood-filled lumens were present, and around the margins of the lesion in the mammary fat there were plump endothelial-lined capillaries and spindle cells in a mass of hemorrhage. In some places the appearances were reminiscent of a cellular capillary angioma, but the more solid areas lacked the differentiation and were probably to be regarded as indicative of a malignant hemangioendothelioma. The tumors were too numerous for surgical excision when the patient was admitted. A test dose of 1,000 r at 140 kv. was delivered in one treatment to one lesion, with no appreciable effect. Diethylstilbestrol (stilbestrol) was also tried in increasing dosage up to 17 mg. per day, without benefit.

From 1925 to 1946 only four cases of hemangioendothelioma were seen and confirmed pathologically in the department of radiation therapy at Bellevue Hospital, New York, together with four other cases in all the other departments of the hospital during the same period, although many thousands of neoplasms were treated in that time. The consensus regarding treatment is that early surgical excision should be followed by irradiation, but opinions vary in regard to the efficacy of radiation therapy.

Histopathology of Cutaneous Lesions in Systemic Lupus Erythematosus. M. Prunieras and H. Montgomery. A. M. A. Arch. Dermat. 74:177-190 (Aug.) 1956 [Chicago].

The authors discuss the newer histopathological and histochemical procedures with regard to the cutaneous lesions of systemic lupus erythematosus. They studied 38 patients with systemic lupus erythematosus and 3 patients with chronic discoid lupus erythematosus. Sections were made from biopsy material fixed in a 10% neutral solution of formalin and embedded in paraffin. The slides were stained routinely by hematoxylin and eosin. The characteristic or diagnostic histological changes in the 38 patients with lupus erythematosus included follicular plugging with hyperkeratosis but without parakeratosis, liquefactive degeneration of the basal layer, and lymphocytic infiltration. Fibrinoid changes in vessels were not frequent (5 of 38 cases), and aggregates of karyorrhexic nuclei were even more infrequent (2 of 38 cases). Distinction between systemic and chronic forms of the disease was found to be almost impossible. The histological changes are related more to the age of the lesions than to the clinical type of the disease, early chronic discoid lupus erythematosus being morphologically indistinguishable from a recent cutaneous manifestation of the systemic form.

Changes in the basement membrane were found, with the aid of the periodic acid-Schiff reaction, to be constant and to be accompanied by an intense macrophagic activity of connective-tissue cells. Fibrinoid changes in the vessels were found less frequently than previous reports would indicate. A positive reaction to Sudan black B that was pyridine resistant was found in five cases; this is possibly related to early senile changes in the connective-tissue fibers. With the methyl green–pyronine stain, controlled by ribonuclease and perchloric acid extraction (modified Brachet test), intracellular bodies termed "red bodies" were found. These bodies represent depolymerization of desoxyribonucleic acid occurring in lymphocytic nuclei. These changes constitute frequent and nonspecific findings. They apparently occur also in the nuclei of connective-tissue cells as a possible early stage in the formation of "hematoxylin bodies." Use of staining with toluidine blue for metachromasia, controlled by use of hyaluronidase, acetylation, sulfation, and oxidation by chromic acid, disclosed preliminary experimental findings suggestive of a pathological modification of the synthesis of mucopolysaccaride by connective-tissue cells in lupus erythematosus.

Kurtin's Surgical Planing Procedure: A Review of Experiences with Special Reference to Post-Acne Scarring. A. A. Small. Canad. M. A. J. 75:279-284 (Aug. 15) 1956 [Toronto, Canada].

Kurtin's surgical planing procedure was practiced in 94 patients, most of whom were treated for postacne pitting. Other conditions were smallpox scarring of 30 years' duration, traumatic scars, tattoos, and even active acne covered with minute sebaceous cysts. Preoperative sedation consisted of 50 mg. of phenobarbital and 50 mg. of meperidine (Demerol) hydrochloride given hypodermically. Prechilling of the face was accomplished with ice packs containing 5% propylene glycol in water. The ice packs were kept in place for 20 minutes in order to remove the initial burning sensation. The field to be treated was delineated with benzalkonium chloride tincture or gentian violet. Ethyl chloride was sprayed on the area and simultaneously a current of air from a blower was directed on to the surface to accelerate the evaporation of the ethyl chloride and thus accelerate the freezing of the skin. The area was frozen so that it was firm to the palpating finger, and the planing was carried out with the Kurtin plastic planer, a small stainless-steel wire brush, disc-shaped and motor driven at 12,000 rpm under control of a foot rheostat. The revolving brush was held vertically against the surface of the skin and was moved fairly rapidly across the area to be planed, with long, firm, uniform strokes. The planing was carried on to the adjacent areas in a systematic manner, and a specific attempt was made to leave no unplaned areas. Usually both cheeks and the forehead were planed during one operation. Perforated Telfa dressings, which combine fabric and plastic materials, were applied to absorb the oozing and early bleeding. The patient was sent home and instructed to remove the dressing after 24 hours, to leave the face exposed to the air during the daytime, and to apply boric acid ointment dressings at bedtime for the first three or four days.

The amount of improvement from a single planing varied in the patients' opinions from 35 to 65%. In patients treated a second and third time, there was usually an additional improvement varying from 10 to 30%. Patients with a round chubby face and a good deal of subcutaneous tissue responded more satisfactorily to the treatment than those whose skin appeared to be closely adherent to the underlying bony structures. Full protection from strong sunlight and wind was essential for about a month after the crust came off, in order to avoid hyperesthesia and mottling of the affected areas. Some patients were subjected to the surgical planing procedure during a period when they had active cystic pustular lesions in some areas, especially along the sides of the neck. All such lesions healed uneventfully. The only precaution taken was the topical use of a mild antibiotic cream for 48 hours over the marsupialized area. The fairly sharp, well-defined, discrete, punched-out acne pit usually lent itself to good results, whereas the deep, poorly defined contracture type of pit that appeared to involve and exert traction on deeper layers of corium was usually much harder to eradicate.

OTOLARYNGOLOGY

Evolution of Surgical Technique in the Treatment of Carcinoma of the Larynx. C. L. Jackson and C. M. Norris. Laryngoscope 66: 1034-1040 (Aug.) 1956 [St. Louis].

Endoscopic excision is the most limited form of partial laryngectomy. Its technique has not undergone any remarkable changes, but the authors reemphasize the importance of the careful selection of cases. Laryngofissure (thyrotomy) is a term that should probably be restricted to the operation of simply splitting the larynx (or rather the thyroid cartilage) in order to gain access to the interior of the larynx for the purpose of removing a tumor and surrounding normal soft tissue. This operation is suitable for very early tumors of one vocal cord. The disrepute into which this operation fell during its early history was due to its misuse in the treatment of tumors that were too extensive and the piecemeal removal of tumor tissue followed by electrocoagulation. A better understanding of the indications for laryngofissure and improvements in technique resulted in its reinstatement. At the Chevalier Jackson clinic of Temple University Hospital the classic laryngofissure operation is still used in cancer involving the middle third of one vocal cord, but a modified form of the anterior commissure operation is employed when the lesion reaches the anterior commissure or crosses over to the opposite cord. In such cases the authors perform a partial laryngectomy with removal of varying amounts of underlying cartilage, an operation perhaps similar to the one Leroux-Robert called "anterior fronto-lateral laryngectomy." The authors also mention Alonso's technique of partial horizontal laryngectomy, which is suitable for limited supraglottic tumors.

Total laryngectomy, like laryngofissure, had a discouraging early history, with a high operative mortality and a high rate of recurrence. Gradually, with improved technique, the operative mortality rate has fallen to almost zero. A simple one-stage excision is now the usual procedure in uncomplicated cases, whereas only a few years ago several leading surgeons advocated a two-stage operation. Whether a vertical or transverse T-shaped or U-shaped incision is used and whether the larynx is removed from below upward or from above downward is a matter of individual preference, sometimes depending upon the location and extent of the tumor. The same may be said of the management of the hyoid bone. Some surgeons simply split it, others remove the body, and still others remove the entire bone. The management of the lymph nodes by "en bloc" dissection of the neck remains the most controversial point. Since only 4% of cordal tumors metastasize and only 10 to 15% of subglottic tumors do so, the surgeon may perhaps be justified in awaiting the appearance of nodes in these cases, but, since about 50% of supraglottic tumors metastasize, he should probably perform a simultaneous "neck dissection" when operating on these tumors, at least on the side of the lesion. When lesions are located anteriorly or bilaterally, it may be difficult to decide upon the side, and perhaps bilateral simultaneous "en bloc" dissection should be considered. The authors have performed more than 50 unilateral simultaneous "en bloc" dissections, but, since all these operations were performed within the past five years, it is not yet possible to give end-results. Summarizing the results in their other patients, they found 79.2% of five-year survivals following surgical treatment (328 of 414 patients). When all patients treated more than five years ago, by surgery and irradiation, are included, the survival rate is 69% (412 out of 593).

The Diagnosis and Treatment of Ménière's Disease. T. E. Walsh. A. M. A. Arch. Otolaryng. 64:118-128 (Aug.) 1956 [Chicago].

Ménière's disease is characterized by vertigo, tinnitus, and perceptive deafness. There is clinical evidence to support the theory that Ménière's disease is the result of vasomotor labyrinthine ischemia. A thorough history and physical examination are required to discover, if possible, allergic, endocrine, and psychosomatic factors that may have etiological significance. Inquiry usually elicits the fact that some hearing loss preceded the onset of vertiginous attacks. The audiometric findings are usually quite characteristic. The patient notices a very definite difference in pitch in the two ears when tested with tuning forks.

The objectives of therapy are to eliminate the vertiginous attacks or, at least, to diminish their intensity and frequency and, if possible, to reverse the hearing loss. Accepting the theory that vasomotor labyrinthine ischemia is due to vasospasm of the cochlear and vestibular vessels, vasodilator drugs have been used in an attempt to control the vertiginous attacks and to improve the hearing. Nicotinic acid in doses sufficient to cause flushing is given three or four times daily. This may be combined with methantheline (Banthine) or propantheline (Pro-Banthine). The author observed amelioration of the vertiginous attacks but no improvement in hearing with these agents. With knowledge of the remarkable effect of 2-acetylamino-1, 3, 4-thiadiazole-5-sulfonamide (Diamox) in glaucoma and in the hope that the secretion of endolymph might be inhibited, just as the secretion of aqueous matter from the ciliary body is inhibited, Walsh used Diamox clinically in a series of patients with Ménière's disease. In two patients there seemed to be a direct relation between the administration of Diamox and the lessening of the vertiginous attacks, but in none was there any appreciable change in the hearing. No one form of medical therapy is effective in all cases. Surgical destruction of the labyrinth gives relief in those cases in which one ear only is affected and should be considered after all medical management has failed.

THERAPEUTICS

Glutamic Acid in Hepatic Coma. N. W. Chaikin, M. S. Konigsberg and M. Schwimmer. Am. J. Gastroenterol. 26: 258-266 (Sept.) 1956 [New York].

Three women and two men between the ages of 42 and 66 years with cirrhosis of the liver and a 15-year-old girl with viral hepatitis became comatose and were treated with glutamic acid given intravenously and orally. An initial dose of 25 gm. of sodium glutamate was given intravenously in 500 cc. of 5% dextrose in distilled water. If the patient failed to regain consciousness within from four to six hours, the dose was repeated. As soon as the patient regained consciousness, the intravenous administration of sodium glutamate was discontinued and 15 mg. of glutamic acid was given twice daily, either orally or by intragastric drip. This was continued until the mental status of the patient was restored to normal. All the patients except the girl with viral hepatitis regained consciousness within 18 hours. The mental state cleared up and improved sufficiently to permit nourishment by mouth. Time was gained to treat the underlying disease more intensively. Administration of glutamic acid did not affect the course of the underlying disease or the results of the liver function tests. In two patients the blood ammonia and pyruvic acid levels were decreased. The exact mechanism by which glutamic acid restores consciousness is not entirely understood. Its beneficial effect may be (1) the result of its ability to unite with ammonia to form glutamine, which in turn is metabolized without the liberation of ammonia; or (2) its ability to combine with pyruvic acid and oxalacetic acid and so prevent ammonia formation.

Gonorrhea: Treatment with a Triple Penicillin Combination. H. R. Wherritt, H. E. Altheide and N. D. Duffett. Missouri Med. 53: 767-768 (Sept.) 1956 [St. Louis].

This study was designed to determine the effectiveness of two formulas, each containing a combination of three penicillin salts, in the treatment of gonorrhea. The original formula identified as Panbiotic provides 300,000 units of buffered potassium penicillin G, 300,000 units of procaine penicillin G, and 600,000 units of benzathine (N, N'-dibenzylethylenediamine) penicillin G per 2 ml. volume. The new formula is the same as the original except that procaine penicillin G has been replaced by the same number of units of dibenzylamine penicillin G. A total of 1,349 patients in whom the diagnosis of gonorrhea was based on a positive smear or culture were treated; 754 received 600,000 units of the new formula of Panbiotic and 595 received 600,000 units of the original Panbiotic. The new formula produced a 98.2% cure rate and the old formula a 98.1% cure rate. These cure rates compared faborably with rates obtained in the treatment of gonorrhea with other penicillin preparations. Only 14 patients showed positive laboratory findings that indicated failure of the treatment. No serious toxic manifestations were observed, and only two minor reactions occurred.

New Perorally Active Penicillin Preparation (Calcipen Leo). E. Henriksen, I. Larsen, E. J. Nielsen, K. Roholt and S. Tybring. Ugesk. læger 118:801-807 (July 12) 1956 (In Danish) [Copenhagen, Denmark].

Clinical investigations show Calcipen (the calcium salt of penicillin V) to be an effective peroral antibiotic in various infectious diseases due to bacteria sensitive to penicillin. Since December, 1955, it has been applied in Blegdam Hospital in 197 patients for whom penicillin was indicated, excluding patients with meningitis, unconscious patients, patients with difficulty in swallowing, and patients with grave gastrointestinal disturbances. The dosage for patients aged over 15 was one Calcipen tablet of 200 mg. every eighth hour daily for six days; for patients aged under 15, it was one half-tablet three times daily for six days. In patients with tonsillitis, scarlet fever, and pneumonia the results of Calcipen treatment equaled those attained by parenteral penicillin treatment. Whether penicillin perorally in the dosage applied is sufficient in treatment of acute suppurative otitis media is not yet certain. In about 7 or 8% of the cases treated there were side-effects, not of a serious kind, partly gastrointestinal, partly in the form of exanthems. As an antibiotic, Calcipen is equal to penicillin G preparation but differs from it in possessing the ability to produce higher serum concentrations.

Anticoagulant Treatment in Acute Coronary Occlusion with Special Reference to Indications. C. Holten. Acta med. scandinav. 135: 15-25 (No. 1) 1956 (In English) [Stockholm, Sweden].

The prognosis of ischemic heart disease, i. e., coronary occlusion, coronary thrombosis, and myocardial infarction, is more favorable now than it was 20 or 25 years ago, but the fact that the mortality rate is still high and the incidence apparently increasing makes the treatment of this condition a matter of outstanding importance. Thrombosis of one or more branches of the coronary arteries is an important but not the only cause of ischemic heart disease; sclerotic occlusion and thrombosis combined with sclerosis are also important, and together these causes account for more than 90% of the cases. The other 10% includes those without distinct infarction or anatomic occlusion and a smaller number in which there is typical infarction but no demonstrable occlusive process in the coronary vessels.

Modern treatment of coronary occlusion is based on the use of drugs that reduce the coagulability of the blood. Effective anticoagulant treatment will counteract the potentially dangerous tendency toward thrombosis found in patients with ischemic heart disease. Formation of the parietal thrombi in myocardial infarction not treated with anticoagulants begins about the fifth day after the onset of the acute attack; therefore, since the effect of the coumarin derivatives takes time to develop, treatment should be started as soon as possible. Heparin, which acts immediately when injected intravenously, may be used to overcome the delay caused by the slowness with which the coumarin derivatives act, but the need for repeated injections and other difficulties connected with the use of this substance in its usual form are distinctly disadvantageous. The author, therefore, in collaboration with the pharmacy of the Municipal Hospital at Aarhus, Denmark, prepared heparin in a sterile solution containing 1.25% carboxymethylcellulose. Each milliliter of this solution, known as Heparin Prolongatum, contains 10,000 international units of heparin. A dose of 2 ml. injected intramuscularly has been shown to prolong the clotting time to 28 or 29 minutes within two hours. The effect is still marked eight hours after a single injection. The solution, which is clear and of low viscosity, can easily be injected with use of a thin cannula. It has been used in 60 patients, 53 with coronary occlusion and 7 with phlebitis, since February, 1955. Altogether about 350 injections have been given; none of the patients had any tenderness at the site of the injections, and no hematomas have as yet appeared.

The first injection of 1.5 or 2 ml. is given as soon as the diagnosis is established, and the second is given eight hours later. Six injections in all are given, the second and subsequent doses being 1 or 1.5 ml. The dosage depends on the estimated weight of the patient. Tests carried out with samples of blood taken at various intervals after the start of the treatment and immediately before the next injection have shown that heparin prolongatum has a satisfactory effect on the clotting time. This application of heparin is an advance in anticoagulant therapy because it is safe and does not cause any discomfort to the patient, the injections can be given by a skilled nurse, and the prolongation of the clotting time is smoothly and evenly attained.

Anticoagulant treatment is indicated whenever ischemic heart disease is present and should be started as soon as the diagnosis has been established, because it is impossible to tell in advance whether the patient will prove to be a good risk or a poor risk. Adequate dosage and daily prothrombin controls are essential if the treatment is to be successful.

PATHOLOGY

Atherosclerosis and Occlusion of the Internal Carotid Artery. K. C. Samuel. J. Path. & Bact. 71:391-401 (April) 1956 [Edinburgh, Scotland].

Both internal carotid arteries were removed in their entirety from the bodies of 82 persons aged, with one exception, from 45 to 91 years. They were studied by the method of frozen sections. Seventy-four subjects revealed atherosclerosis of some degree, including 15 cases of severe atheroma. Severe grades of atherosclerosis were seen twice as often in men as in women. Complete occlusion of one carotid artery was seen in five cases; the internal carotid in four and the common carotid artery in one. Two of these occlusions were due to recent thrombus, one to an organizing thrombus, and two to atherosclerosis alone. Thrombosis in each case had occurred on the left side.

Atherosclerosis was the only arterial disease observed. Thrombosis appeared to be a complication of it. Three cases of severe atherosclerosis showed foreign-body giant-cell reaction around cholesterol crystals. It was thought that two different forms of atherosclerosis could be seen: fatty changes in mural thrombi and pure lipoid deposits by cholesterophages. The site of most severe involvement was found to be the sinus portion of the artery. Next in order of frequency were the cavernous, cerebral, petrous, and cervical portions. In one case the artery was occluded in the petrous portion. Brain lesions were variable but were present in most cases of severe atherosclerosis. They probably depend on the patency of the opposite carotid artery, and on the collateral circulation through the circle of Willis. Their symptomatology was varied. Mental confusion, dizziness, dementia, and hemiplegia were especially noted. Symptoms were absent in one case in spite of complete occlusion of one internal carotid artery. Occlusion or narrowing of the internal carotid arteries from atherosclerosis should be considered among the causes of mental or neurological symptoms in elderly persons.

PHYSIOLOGY

Cholinergic Innervation of the Digital Arteriovenous Anastomoses of Human Skin: A Histochemical Localization of Cholinesterase. H. J. Hurley Jr. and H. Mescon. J. Appl. Physiol. 9: 82-84 (July) 1956 [Washington, D. C.].

Six-millimeter punch biopsies were taken from the skin of the volar pads of the great toes of five healthy, white, male volunteers (22 to 25 years of age) after block anesthesia of the digit with a 1% procaine solution. The technique of Koelle, using the latest modifications described for the localization of specific and nonspecific cholinesterase, was then employed on fresh frozen sections (10-μ thickness) of these specimens. Specific cholinesterase was found in many nerve fibers about the specialized arteriovenous anastomoses of digital skin and about the secretory tubules of eccrine sweat glands. The enzyme was absent about other cutanous vessels and the ducts of the sweat glands. No significant concentrations of nonspecific cholinesterase were detected about any of these structures. The presence of specific cholinesterase about the digital arteriovenous anastomoses indicates that these vessels possess a cholinergic innervation. On the basis of cited pharmacological evidence, it is suggested that this innervation is vasodilatory.

Effect of Amino Acid and Glucose Ingestion on Arteriovenous Blood Sugar and Appetite. S. M. Mellinkoff, M. Frankland and M. Greipel. J. Appl. Physiol. 9: 85-87 (July) 1956 [Washington, D. C.].

When healthy persons ingest whole or hydrolyzed protein, appetite diminishes as the serum amino acid concentration rises and vice versa. The same inverse relationship appears after the infusion of amino acids despite the fact that both infusion and ingestion of amino acids cause the blood sugar level to fall. Thus, appetite is depressed when the blood sugar level is low, and a recrudescence of appetite is accompanied by a rising blood sugar level. Mayer suggested that the metabolic regulation of the appetite might be explained by nervous centers that are responsive to changes in the arteriovenous (a-v) differences in blood sugar. The effect of amino acid ingestion upon the arteriovenous blood sugar difference was investigated in 16 normal volunteers. After the usual nocturnal fast, they drank 250 cc. of 10% amino acids. Blood specimens were obtained from the antecubital vein and from one of the finger tips in the fasting state, 30 minutes after the test meal, and at hourly intervals after the test meal for a period of four hours. As a means of comparison, the procedure described above was followed in 10 normal volunteers, but a solution of glucose was used as the test meal instead of amino acids. The following were serially estimated: (a) serum amino acid nitrogen, (b) venous and capillary blood sugar, and (c) desire for food.

After the ingestion of amino acids, the blood amino acid concentration and the arteriovenous blood sugar difference increased, while the venous blood sugar level and the appetite fell. After the ingestion of glucose, appetite varied inversely with the arteriovenous blood sugar difference, but there was no correlation between appetite and the serum amino acid concentration. There was a considerable range in the fasting arteriovenous sugar difference in these healthy persons. Thus an arteriovenous sugar difference of 8 mg. per 100 cc. one hour after the test meal in one individual represented an increase in the arteriovenous sugar difference of 8 mg. per 100 cc., while in another individual the same one-hour value represented an insignificant increase of 2 mg. per 100 cc. Nothing in these simple experiments can be construed as proof or disproof of Mayer's arteriovenous sugar hypothesis, but the data are not inconsistent with this hypothesis. The fact that the venous blood sugar level was generally lowest when the arteriovenous sugar difference was greatest suggests that one mechanism for depressing the venous blood sugar level after ingestion of amino acids is uptake of glucose by the muscles. That this mechanism is probably not the only one operative is suggested by the fact that in some individuals a significant fall in the venous blood sugar level occurred without any real change in the arteriovenous sugar difference. In the latter circumstance, presumably the glucose was taken up by the liver.

Studies on the Physiology of Hunger: I. The Effect of Intravenous Administration of Glucose on Gastric Hunger Contractions in Man. A. J. Stunkard and H. G. Wolff. J. Clin. Invest. 35: 954-963 (Sept.) 1956 [New York].

The observation that the intravenous administration of glucose could abolish gastric hunger contractions in fasting dogs led Bulatao and Carlson to postulate that lack of availability of carbohydrates for utilization is an important factor in the genesis of the gastric hunger contractions. Recently this problem was reopened by Mayer's "glucostatic" theory of the regulation of food intake, which ascribes hunger to a depletion of the carbohydrate stores of the body and satiety to the replenishment of these stores. According to this theory, the status of the carbohydrate stores is signalled to the hypothalamic food-regulatory centers by the rate at which glucose is utilized. To obtain more information on the effects of glucose on gastric hunger contraction the authors investigated the capillary-venous glucose differences in fasting subjects and after the injection of glucose.

They found that intravenous administration of 50 ml. of a 50% solution of glucose was followed within five minutes by the cessation of gastric hunger contractions in 19 of 40 experiments on a group of diabetic and nondiabetic human subjects. At 10 and 20 minutes after injection, the peripheral capillary-venous glucose differences in the group of 19 subjects in whom contractions were inhibited were significantly higher than those of the subjects in whom contractions persisted. In 14 of the 19 experiments in which contractions were inhibited, they returned at an average of 47 minutes after the injection. The capillary-venous glucose differences at 10 and 20 minutes after injection were usually higher than those at the time contractions returned, but this difference was not significant at the 5% level. The capillary-venous glucose differences in the 5 experiments in which contractions remained inhibited were significantly higher than those in the 14 experiments in which they returned. These findings support the view that metabolic events accompanying increased peripheral removal of glucose have an inhibiting effect on gastric hunger contractions. Events associated with decreased removal, on the other hand, are not a sufficient stimulus for the production of gastric hunger contractions, although they appear to be a necessary condition.

BOOK REVIEWS

Treatment of Heart Disease: A Clinical Physiologic Approach. By Harry Gross, M.D., F.A.C.P., Attending Physician, Montefiore Hospital, and Abraham Jezer, M.D., Attending Physician, Montefiore Hospital, New York. Cloth. $13. Pp. 549, with 91 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, England, 1956.

According to the authors, this book was added to the numerous recent books on heart disease as a "presentation of therapy in heart disease based upon sound physiological principles." Actually, the volume contains a great deal of information regarding symptomatology and diagnosis of the various forms of heart disease in addition to the discussion of therapy. The book is divided into seven parts. The first deals with the general aspects of pathological physiology of the circulation and with the action and clinical use of digitalis and quinidine sulfate; the subsequent sections deal with the pathogenesis, diagnosis, and management of hypertensive and arteriosclerotic heart disease, heart disease secondary to inflammation, congenital heart disease, surgery and pregnancy in heart disease, heart disease secondary to metabolic disorders, and the psychosomatic aspects and rehabilitation of patients with heart disease. A well-chosen list of references is included after each chapter, and at the end there is a useful appendix containing diets, recipes, and tables of the sodium and potassium contents of foods.

By and large, indications to medical and surgical therapy and details of the therapeutic management are well presented. It is to be hoped that in future editions the chapter on treatment of acute pericarditis will be expanded and will include treatment of tuberculous pericarditis. Occasional inconsistencies should be eliminated; for example, in the chapter on paroxysmal tachycardia it is first stated—and rightly so—that variations of the first heart sound do not permit one to differentiate between supraventricular and ventricular tachycardia, but later the same phenomenon is referred to for the differentiation of the two types of paroxysmal tachycardia. Slowing of the heart rate by quinidine in sinus tachycardia is mentioned and explained as a vagal effect on the sinus code. Actually, the vagal effect of quinidine consists in an atropine-like action. Of the drugs to be used to abolish premature beats, digitalis is listed first and quinidine second. Procaineamide hydrochloride is not mentioned at all. This order of efficacy can be questioned. Exception can be taken to the statement that electrically induced pulsus alternans is "one of the few pathognomonic signs of digitalis poisoning." It is regrettable that a number of the illustrations show some of the electrocardiograms upside down, as in figures 14, 33, 46, and 48, or mislabeled, as in figure 40. In spite of such minor flaws the book can be recommended both to the general practitioner and to the internist as a competent, up-to-date textbook on cardiac therapy written by two authors familiar with the literature, guided by an extensive experience of their own, and exhibiting a rather essential attribute of a good therapist: common sense.

The Doctor in Personal Injury Cases. By Harold A. Liebenson. Cloth. $4. Pp. 123. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1956.

With the ever-increasing number of claims and suits requiring written reports or testimony from physicians, it is important for attorneys to take the time and effort to help the medical profession understand the proper form and the significance of the evidence or testimony they are called on to present. This book is a conscientious effort on the part of an experienced trial attorney to pass on his experiences and suggestions to physicians and attorneys. The book is a short, concise, simply worded and welcome addition to medicolegal literature.

The glossary of legal terms is short, yet sufficient to meet the needs of most physicians. The description of the conduct of a trial, the legal rules governing the admissability of opinion evidence, and the discussion of the purpose and form of hypothetical questions should be particularly helpful and informative to the medical profession. In all probability, however, the most significant contribution that the book provides is in connection with medical reports. Despite the frequent demands on physicians for such reports, there is a surprising lack of understanding as to their proper form and their tremendous importance in the equitable settlement of claims. If the suggestions presented concerning the preparation of medical reports and the proper demeanor of a medical witness in court would be read and followed, the time, patience, and reputation of many physicians would be saved. In addition, and most important, many cases could be settled equitably prior to trial, and those that did go to trial would be decided on full, complete, and unbiased medical facts.

Occasionally the author has mistakenly portrayed the physician or medical witness as an advocate rather than as an unbiased reporter of facts in the personal injury case. On page 5 he says: "Once the doctor realizes and understands his importance in these cases, half the battle of winning personal injury cases is over." What he means is that half the battle of obtaining justice is over—a result that does not always mean "winning" a personal injury case. Again, on page 6, in discussing the causal connection between the alleged injury and the accident, he says: "At trial the doctor must prove this point." Actually, the testimony of the physician may either prove or disprove this point. Any burden of proof that exists is on the plaintiff and his attorney—not the physician. This book has nine chapters. It should have stopped at eight. It is inevitable that any attempt to discuss malpractice, privileged communications, workmen's compensation, subpoena, and *subpoena duces tecum* in five and one-half pages will result in inaccuracies, misstatements, and false impressions. Chapter 9 is no exception. The rest of the book, however, is well written and informative, and, as stated, in the foreword, "is a worthwhile addition to the physician's and lawyer's library."

Otolaryngology. Volumes 1-5; General Index. Edited by George Morrison Coates, A.B., M.D., Consulting Otolaryngologist, Hospital and Graduate Hospital of University of Pennsylvania, Harry P. Schenck, B.S., M.D., Professor and Head of Department of Otolaryngology, University of Pennsylvania School of Medicine, and M. Valentine Miller, B.S., M.D., Sc.D., Professor of Clinical Otolaryngology, Graduate School of Medicine, University of Pennsylvania, Philadelphia. Cloth, loose-leaf. $105 [which includes service of new pages and Consulting Bureau for one year] .Various pagination, with illustrations. W. F. Prior Company, Inc., P. O. Box 350, Hagerstown, Md., 1956.

Attractive in appearance, beautifully illustrated, and smoothly edited, this large work consists of the contributions of 118 distinguished specialists in fields relating to the ear, nose, and throat.

Volume 1 deals especially with the anatomy, physiology, anomalies, and diseases of the external ear; with otitis media; and with tinnitus, vertigo, and deafness. Volume 2 continues with otosclerosis and fenestration, mastoiditis and mastoidectomy, audiology and the rehabilitation of the deaf, and the treatment of certain tumors and infections. Volume 3 deals mainly with the nose and the accessory sinuses, their diseases (including allergies), and their surgical and radiological treatment. Volume 4 is devoted mainly to the mouth, pharynx, and larynx and contains valuable contributions on bronchoscopy. Volume 5 contains chapters on the esophagus, on the removal of foreign bodies from the respiratory and upper gastrointestinal tract, on speech difficulties and the relearning of speech after laryngectomy, and on the other sciences and specialties relating to otolaryngology. The chapter on pharmacology is particularly valuable because of the concreteness of the information, especially in regard to dosage. While the contributions vary somewhat in quality, most are critical and up-to-date, and some deserve to become classics. An excellent system of numbering the pages makes it easy to locate the passages referred to by the index. This is vital not only because of the loose-leaf plan of the volumes but also because of the multiple authorship, which has evidently made it hard to follow a completely logical plan in arranging successive chapters. The index still leaves much to be desired, however. It does not

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enable one to locate, for instance, the important material on cholesteatoma given in volume 1 (chapter 10, page 78) or the material and illustration on actinomycosis found in volume 2 (chapter 26, page 9). This defect can easily be remedied in a book that is intended to be, and deserves to be, a continuing project.

Cardiac Pressures and Pulses: A Manual of Right and Left Heart Catheterization. By Aldo A. Luisada, M.D., Associate Professor of Medicine, Chicago Medical School, and Chi Kong Liu, M.D., Instructor of Medicine, Chicago Medical School, Chicago. Cloth. $6. Pp. 116, with 51 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 99 Great Russell St., London, W.C.1, England, 1956.

Since cardiac catheterization has become a well-recognized diagnostic procedure, such a book as this, describing the techniques in detail, is most welcome. It was only a little more than a decade ago that Cournand showed that catheterization of the right side of the heart could be safely performed in man. Since then, many improvements in recording instruments and in the technique itself have been made. Recently, relatively safe techniques for catheterization of the left side of the heart have been made available. The procedures are all carefully described in this book. The authors, who have had extensive experience with the techniques, emphasize the necessity for a good, well-trained team of from four to eight persons in order to get the necessary information from the tests. One person passes the catheter, another takes care of the recording instruments, another handles the x-ray apparatus, and another collects the blood samples. Occasionally additional personnel, such as a nurse, an anesthetist, a surgeon, or an additional technician, may be necessary. The procedures are described in detail, step by step, and attention is called to faults in technique that might increase the risk to the patient or give unsatisfactory results. Much space is allotted to artefacts and how they may be prevented. This section is important, because the presence of artefacts in the records obtained could lead to faulty and inaccurate interpretations. The book is well illustrated. It is recommended as an excellent reference book not only for the physician who actually does cardiac catheterization but also for those who interpret the data obtained from such studies. It is a book that every cardiologist should have in his library for ready reference.

Hutchison's Food and the Principles of Dietetics. Revised by V. H. Mottram, M.A., and George Graham, M.A., M.D., F.R.C.P., Consulting Physician to St. Bartholomew's Hospital, London, England. Eleventh edition. Cloth. $8.25. Pp. 630, with 17 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2; Edward Arnold & Co., 41-43 Maddox St., London, W.1, England, 1956.

Those who have a special interest in foods, diet, and nutrition will find interesting reading in this book, but those who want a concise reference on the subject should consult the standard works written by investigators in the United States. No objection is taken to the reliability or authoritativeness of the book, but, as it was written for use in England, the physician and nutritionist in the United States is likely to find it confusing.

Anatomical Atlas of the Human Brain and Spinal Cord. By Mieczysław Stelmasiak, M.D., Professor of Human Anatomy, Medical Academy, Lublin. Translated by F. Stański, M.D., from second Polish edition. Cloth. Pp. 227, with 241 plates. Polish State Medical Publishers, Principal Medical Library, 22 Chocimska, Warsaw, Poland, 1956.

This atlas is an English translation prepared from the second Polish edition, which appeared in 1953. Russian and German translations are said to be in preparation. Professor Stelmasiak of the Medical Academy of Lublin has used the *Nomina Anatomica* adopted in 1955 by the sixth International Anatomical Congress at Paris. The book is a true atlas, without text except for figure legends. It consists of diagrams (a few in color), drawings, photographs, and charts of neural pathways. Diagrams are well reproduced but oversimplified. Photographs of transverse and sagittal sections of the brain stem and cerebellum, and transverse, sagittal, and horizontal sections of the cerebrum, form the greater part of the atlas. These illustrations are poorly reproduced and are lacking in contrast, definition, and detail. It is unfortunate that black backgrounds were used throughout for these photographs. Photographs of the brain are well reproduced and clearly labeled. Most of the drawings appeared idealized and unreal. A section of the atlas devoted to craniocerebral topography contains photographs of the head sectioned in various planes. The value of such photographs is questionable. The size and probably the cost of the atlas could have been reduced by better use of space. About 100 of the 218 pages contain illustrations occupying only half of the page. This atlas is not equal in any respect to Riley's "Atlas of the Basal Ganglia, Brain Stem and Spinal Cord," which is so highly regarded by most students of the nervous system. Most of the standard neuroanatomic textbooks used by students in the United States provide better and more detailed illustrations of the nervous system.

Muscle Testing: Techniques of Manual Examination. By Lucille Daniels, M.A., Associate Professor and Director of Physical Therapy, Department of Allied Medical Sciences, School of Medicine, Stanford University, San Francisco, Marian Williams, Ph.D., Assistant Professor of Physical Therapy, Stanford University, and Catherine Worthingham, Ph.D., Director of Professional Education, National Foundation for Infantile Paralysis, Inc. Second edition. Paper. $4. Pp. 176, with format and test illustrations by Harold Black; anatomic drawings by Lorene Sigal. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, England, 1956.

This book offers a wealth of accurate anatomic and kinesiological information, in the form of text and line-drawings, for use in testing and recording the status of individual muscles in patients with various forms of neuromuscular disability. The material is often rendered unclear by the use of a telegraphic style, but the illustrations are excellent. Commendable effort has been put into a comparative study of other proposed methods of grading manual muscle tests, but much work along this line remains to be done. Bovard and Cozens have shown that a given mass of data can generally be scored in many ways but that the various ways can be compared systematically as to their dependability by computing reliability indexes from test-retest data. The choice of the best possible method of scoring becomes extremely important in any situation that involves questions of employability or compensation. It is hoped that the authors will continue their good work in this direction. The book lacks an index, but it has a good bibliography.

Understanding Human Behavior. By James L. McCartney, M.D., F.A.C.P. Cloth. $3.50. Pp. 258, with 12 illustrations. Vantage Press, Inc., 120 W. 31st St., New York 1, 1956.

This book is clearly written and presents in 10 well-organized chapters adequate information to the intelligent layman about the current neuropsychiatric theories and practices. Its lucid style, unbiased approach, and hopeful outlook into "a philosophy of living" make it a worthwhile addition to the available literature. In dealing with normal and abnormal sexual behavior, the author's long psychiatric experience leads to thoughtful evaluations. The chapter on diagnosis aptly describes the many psychic reactions and disorders, but it is weighed down by a long list of the standard nomenclature of the American Psychiatric Association and too much emphasis on electroencephalographic studies. This results in scant information about important psychometric and projective test methods. The chapters about origin of frustration, origin of guilt, psychotherapy, and physical treatments make fine introductory reading for medical students and nurses. A glossary and index complete this useful book.

Poliomyelitis. By W. Ritchie Russell, C.B.E., M.D., D.Sc., Director, Department of Neurology, United Oxford Hospitals, Oxford, England. Second edition. Cloth. $3. Pp. 147, with 40 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2; Edward Arnold & Co., 41-43 Maddox St., London, W.1, England, 1956.

This monograph constitutes an extensive review of the literature. It is well arranged, with a good table of contents for ready reference, and should be of value to clinicians who have occasion to see patients for diagnosis or treatment. The discussion on the treatment of respiratory paralysis in spinal cases perhaps gives undue emphasis to the European's conception of respiratory devices, namely, the use of positive pressure; however, due recognition is given to American methods of treatment. In fact, the advantages and disadvantages of both concepts of treatment are presented quite fairly. In the final chapter, on future prospects, the continued reluctance on the part of the British to recognize the value of inactivated virus vaccine is apparent; and the summary indicates an undue reliance on the early availability of a live virus vaccine. Advances in treatment are so rapid that this monograph will soon be out-of-date.

QUERIES AND MINOR NOTES

EXCESSIVE X-RAY EXPOSURE

To the Editor:—*A man was given a diagnosis of duodenal ulcer while in the Army in 1925. He left the service in 1927 and was examined by the Veterans Administration in 1932 and then no more until 1947. These examinations included gastrointestinal x-ray series. Since 1953, the VA facility has what is now termed an ulcer clinic. Routine blood and urine examinations plus chest x-ray and gastrointestinal series were performed three times in 1954, twice in 1955, and once so far in 1956—with another scheduled in six months. Apparently this procedure is to go on indefinitely. Is this too frequent x-ray exposure?* *M.D., Texas.*

Answer.—It is not believed that the gastrointestinal examinations made prior to 1953 were too frequent. Since 1954, the patient has had six complete gastrointestinal examinations. Two series in one year is believed to be within safe limits, if the examinations are not carried out over a number of years. It is also important that the fluoroscopist does not consume too much time or that an excess of spot films are not made during the examination. The usual fluoroscopic factors are 80 kv. peak, 5 ma., 1 mm. of aluminum filter, 13 in.-target tabletop distance. With these factors, the intensity is approximately 7 r per minute. The factors used in making spot films are 80 kv. peak, 150 ma., 1 mm. of aluminum, 13 in.-target tabletop distance. Intensity is 4 r per second or 240 r per minute. If the usual number of films are exposed, plus the fluoroscopic and spot films, the patient received in the neighborhood of 67 r. Gallbladder examination is not included in this estimate. Three complete gastrointestinal examinations as a yearly plan is beyond the safe limits and is not necessary. One gastrointestinal x-ray examination a year to check a duodenal ulcer should be enough, unless an emergency arises. Much has been written lately on the deleterious effects of irradiation on the gonads and also about the effect upon the blood cells. It is safe to carry out x-ray examinations when needed, provided the radiologist is familiar with the output of his machines. One should be very careful, especially in examining youngsters, as mutation with gradual evolution and alteration in heredity and in the germ plasm may become evident in later generations.

PAINT REMOVERS

To the Editor:—*A patient, aged 48, complains of having been extremely tired at night for the past nine months. During this time, he intermittently used a paint and varnish remover that contained methylene chloride. The blood cell count was as follows: hemoglobin level, 13 gm. per 100 cc.; red blood cell count, 4,600,000 per cubic millimeter; hematocrit, 44%; white blood cell count, 9,600 per cubic millimeter; total neutrophils, 67%; lymphocytes, 29%; eosinophils, 1%; monocytes, 3%. Blood chemistry studies were as follows: blood sugar level, 103 mg. per 100cc.; urea nitrogen level, 14 mg. per 100 cc.; cholesterol level, 200 mg. per 100 cc.; cholesterol esters, 70%; calcium level, 10.7 mg. per 100 cc.; phosphorus level, 3.1 mg. per 100 cc.; total protein level, 6.1 gm. per 100 cc.; albumin level, 3.8 gm. per 100 cc.; globulin level, 2.3 gm. per 100 cc.; thymol turbidity, 1.2 units; cephalin flocculation test, negative; alkaline phosphatase, 1.0 Bodansky units; acid phosphatase, 0.3 Bodansky units; and Kahn test, negative. Would this solvent produce such clinical findings?* *M.D., New York.*

Answer.—This query fails to provide any substantial information as to the extent of exposure. "Intermittently" is subject to endless variation. No precise opinion in reply is warranted. In general, currently applied paint removers fall into two categories. The long-used ones contain benzene (benzol) along with acetone, methanol, and paraffin wax. The paraffin and acetone constitute minor affronts to health, systemic methanol poisoning is practically unknown from industrial exposure, but the benzene is highly toxic and the conditions of applying paint remover are conducive to severe exposure. Yet the laboratory picture provided is not descriptive of benzene poisoning. Shortly after exposure to benzene the fact of exposure may be established by the readily conducted urine-sulfate test, which, when positive, is characteristic of benzene exposure but not of benzene poisoning. The newer paint removers are likely to contain methylene chloride as the chief constituent along with paraffin or methyl cellulose and some solvent less evaporable than methylene chloride such as toluene (toluol). Collier, cited by Browning (Toxicity of Industrial Organic Solvents, rev. ed., London, Her Majesty's Stationery Office, 1953, p. 123), describes a series of intoxications from methylene chloride present in paint removers. He notes: "The symptoms in the two most severely affected patients who had to leave work were, however, largely subjective, and the evidence was rendered to some extent indefinite by the presence of intercurrent affections, lead poisoning in the one and duodenal ulcer in the other. The first complained of irregular but severe pains in legs and arms, hot flushes, headache, vertigo, stupidity while at work, difficulty in reading on account of eyesight not being clear, anorexia, precordial pain, rapid pulse, shortness of breath, fatigue on exertion and attacks of rapid beating of the heart. No objective abnormalities were present with the exception of haematological changes including slight anaemia and punctate basophilia, attributable to his previous exposure to lead. In the second case the subjective symptoms were very slight, e. g., drowsiness, pains in the head, irritability and tingling in the hands and feet, and a diagnosis of gastro-duodenal ulcer was made on admission to hospital." However, the present-day consensus is that methylene chloride as applied in industry is relatively harmless. It may be noted that "fatigue" appears in the list of subjectives symptoms.

DRINKING WATER WITH A LOW pH

To the Editor:—*In this area there are many instances of drinking water with a low pH, as determined by an independent laboratory. Several statements by those supposedly well informed indicate that a pH reading of 6.5, or lower, in drinking water might cause tooth decay, gallstones, kidney stones, and nonspecific "indigestion." Please enlighten us on this matter.* *John W. Nance, M.D., Clinton, N. C.*

This inquiry was referred to two consultants whose respective replies follow.—Ed.

Answer.—The pH is not a specific entity but is a measure of the degree of acidity or alkalinity. Many natural waters have an acid reaction, while others have an alkaline reaction. In general, the compounds that cause acidity (pH 6.9 and lower) are some form of sulfur, chlorine, phosphorus, or organic acids. Those compounds that cause alkalinity (pH 7.1 and higher) are principally calcium, magnesium, potassium, and the carbonates. A pH of 6.0 to 6.9 is only very slightly acid. Most distilled waters fall into this pH range. With the possible exception of tooth decay, none of the conditions named appear to be related to the pH of drinking water. In regard to tooth decay, there should be

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

no concern over a water supply until the pH falls to at least pH 5.0. Exposure to water supplies with a lower pH (below 5.0) over a prolonged period of time might possibly have some decalcification effect on enamel.

Answer.—Adequate data are not available on the health hazard of consuming waters of low pH value. However, many common canned foods and beverages have lower pH values than most potable waters. The following table gives representative pH values of some common canned or bottled foods.

Canned Foods	Representative pH Value	Canned Foods	Representative pH Value
Apples	3.4	Grapefruit juice	3.3
Asparagus	5.5	Lemon juice	2.4
Beans, green	5.7	Milk, evaporated	6.2
Carbonated beverages	<3.0	Peaches	3.8
Carrots	5.2	Potatoes, white	5.5
Cherries, red	3.5	Spaghetti in tomato sauce	5.1
Coffee	5.5	Tomatoes	4.3
Corn	6.1		

Also it is important to remember that stomach contents normally range from a pH of 3 to 6.8.

In view of the relatively low pH of much of our food and of the excellent buffering properties of gastric and duodenal juices, it seems unlikely that drinking water with a low pH value (such as 5.5-6.5) could be significant in producing gallstones, kidney stones, or "indigestion."

There is some disagreement among dentists as to the existence of an association between consumption of lemon juice and the production of dental caries. Lemon juice has a much lower pH than most potable waters. It seems unlikely, then, that drinking waters with pH values falling within the range commonly found in unpolluted waters have the effects mentioned in this query.

TELEVISION

To the Editor:—*Are there any glasses especially helpful in viewing television? I have many complaints of discomfort of that kind.*

M.D., Maine.

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—Television should cause no ocular discomfort in healthy eyes if the image is clear and viewed with the proper correction and with the proper distribution of illumination in the room. Watching the screen in a completely dark room is undesirable, as central glare then results and the image may lose sharpness because of pupillary dilatation. Only clear distance-vision glasses should be used. Tinted lenses of any type whatsoever reduce the light entering the eye and are hence detrimental. But lenses with antireflection coating of magnesium fluoride admit more light to the eye and consequently should add to the clarity of the view. When discomfort arises, the most common cause is conjunctival asthenopia. The conjunctival hyperemia usually responds to instillations of zinc sulfate, ½%; cold compresses; and, if necessary, eye drops of epinephrine chloride (1:1,000). The corticosteroid eye solutions are also effective.

Answer.—There are no unusual conditions in viewing television that require special glasses. Most television sets are adjustable as to position, distance from the viewer, brightness, contrast, and focus. In some localities the view is variable due to interference beyond control of the viewer. When conditions are adjusted to the best possible extent by the viewer for his comfort, including eye comfort, one should be able to view the picture without unusual eye strain. At the optimum distance for viewing television, 15 ft. or more, only distance glasses are used. For those who need to wear glasses for distance, the same correction is worn for television. There is nothing to be gained by wearing tinted glasses, filters, or other optical appliances while viewing television that are not used for full-time wearing of glasses for distance. It is not advisable for adults to view television for longer than a few minutes at distances less than 12 ft.

HYPNOSIS AND CHOREA

To the Editor:—*Can the physical movements of Sydenham's chorea be removed during hypnosis? Also, since the movements of Sydenham's chorea disappear in sleep, will they disappear in a sleep-like hypnotic trance? If the movements of chorea can be removed temporarily for the duration of a hypnotic trance, does it prove that this is actually psychogenic chorea and not Sydenham's chorea?*

M.D., Missouri.

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—Since choreic movements are greatly affected by the emotional state of the patient, it is difficult to determine how much of the condition is actually due to organic disease. Without a detailed history it would be difficult to come to a conclusion as to whether the symptoms are primarily psychogenic. It is a well-known fact that the conscious part of the brain is placed at rest during sleep, while the unconscious continues in activity. Many experiments have been carried out that indicate that persons suffering from chorea of one form or another will have a disappearance of symptoms while under the effects of hypnosis, as they do while in natural sleep. If the hypnotic treatment is continued over a period of months and frequently repeated, the will to control the movements becomes increasingly effective. The therapeutic value of hypnosis depends on posthypnotic suggestion. Consequently, if the will to control is well implanted in a person's mind, it is quite possible that the effects of the suggestion may be continued over an extended period. On the other hand, it should be remembered that hypnosis is not a permanent method of cure. Without adequate insight, hysterical reactions may return if the patient is under sufficient stress. One or two treatments under hypnosis is not an adequate test in evaluating this type of treatment.

Answer.—The temporary cessation of the choreal movements during the hypnotic trance does not rule out Sydenham's chorea, since hypnosis and/or strong suggestion reduces tremors and other movements, such as ballism or tics, of basal ganglionic origin. Inasmuch as peripheral chronaxy is heightened and lowered by suggestion, nerve function can be improved by scientifically applied suggestion-hypnosis, thus hastening the recovery of patients, especially those with the reversible neuropathological changes that characterize Sydenham's chorea.

TISSUE STAINING FOR AMYLOIDOSIS

To the Editor:—*Please suggest the most efficient staining techniques for demonstrating primary amyloidosis.*

Harry Shecter, M.D., Philadelphia.

Answer.—Variations in the staining reactions of amyloid and in the intensity of color absorption with specific stains is commonly observed in primary systemic amyloidosis. Therefore, several staining procedures should be used. Fixation of the tissues in a 10% formaldehyde solution or absolute alcohol is prescribed, but good results are obtained with tissues fixed in Zenker's solution. A permanent efficient procedure is with the crystal violet stain (Lieb: *Am. J. Clin. Path.* 17:413, 1947). Deparaffinized sections are immersed in about 0.3% crystal violet solution for one to three minutes (10 cc. of saturated alcoholic crystal violet solution in 1 cc. of hydrochloric acid and 300 cc. of distilled water; the stock crystal violet solution consists of 14% crystal violet in 95% alcohol). Check under the microscope. Rinse well in tap water and mount from water in a solution of 50 gm. of Abopon and 25 cc. of distilled water. (Abopon is a water-soluble synthetic resin, available from Glyco Products Co., 148 Lafayette St., New York. Mix Abopon with water under heat.) The amyloid becomes purplish-red (violet), while other tissue elements are stained blue. The shade of the violet varies. A second good method is Bennhold's Congo red stain (*München. med. Wchnschr.* 69:1537, 1922). It stains amyloid pale pink to red in frozen, paraffin, or celloidin sections. Stain slides in a 1% aqueous solution of Congo red for 10 to 30 minutes, or longer if a deep color is desired. Dip the sections in a saturated aqueous solution of lithium carbonate for 15 seconds; decolorize in 80% alcohol until the stain no longer is removed. Wash in water for 15 minutes, counterstain with alum hematoxylin for 1 to 2 minutes, wash in water, dehydrate in 95% and absolute alcohol, xylene (xylol), and mount in balsam. If substances thought to be amyloid fail to give these staining reactions, one of the collagen stains to differentiate amyloid from ordinary hyalin can be used.

RECURRENCE OF HERPES ZOSTER IN THE SAME AREA

To the Editor:—*A 36-year-old woman has periodic recurrence of almost typical herpes zoster of the zygomatic branch of the trigeminal nerve. The attacks began about eight years ago, coming on each year at first, then twice each year, and now every three or four years. The lesion this time consisted of typical clusters of herpetic lesions over the zygomatic branch, left side, with edema of the cheek and enlargement of the corresponding cervical lymph node. Tenderness was in the supraorbital and infraorbital nerves. Twice she says she had extension of the lesion into the conjunctiva of the eye. Blood cell count, Kahn test, and urine examinations were normal. X-ray pictures of sinuses showed nothing abnormal. The symptoms follow a fixed routine, being very similar each time. Between attacks she has no symptoms. There is no sensory or motor disturbance except the pain. Does herpes zoster recur in the same location? What type of focal irritation to the root could repeat in this manner? Is there any treatment to prevent recurrence?* *John D. Gleckler, M.D., Denison, Texas.*

Answer.—Instances of herpes zoster in which the condition recurs periodically at the same site have been observed, but many authorities express the belief that in such cases the condition is really a herpes simplex, even though it does appear to follow a specific nerve root distribution. It is often stated that herpes zoster may be either idiopathic or symptomatic and that in the latter type some local lesion of the nerve roots or systemic disease may serve to activate the infection and determine the site of involvement. Carcinoma, Hodgkin's disease, and leukemia are frequent etiological agents in this latter type. Search should be made for both systemic disease and focal irritation or disease in the region of sensory roots of the left trigeminal nerve.

HEMORRHAGE AFTER TONSILLECTOMY

To the Editor:—*How could one detect post-tonsillectomy hemorrhage before signs of shock develop in a child who is still unconscious from anesthesia?*

Jacob Greenblatt, M.D., Stamford, Conn.

Answer.—Because no statement of details about premedication and anesthesia is given, an answer must be in general terms. Preoperative sedation should be carried out about two hours previous to the intervention. It is true that the effect will not be as pronounced as when given one hour previously, but the calming influence will still be there and the patient will stir much sooner. All doses should be calculated for the individual patient concerned. The general anesthetic (usually ether) should be so given that the child will react and vomit shortly after the surgeon is through and while the patient is still on the operating table. Hemostasis should be meticulous. Patients treated as outlined above, even if they bleed, will be so far awake that all fresh blood from the nose and mouth will be quickly visible and act as a warning; furthermore vomiting will take place early, before much blood loss. It is the deeply narcotized and anesthetized patient who acts as described above, and the taking of blood pressure readings will be an unsatisfactory safeguard. It goes without saying that a properly trained attendant should be constantly present with children returned to their rooms after tonsillectomy.

ICE BAGS APPLIED TO CHEST FOR HEMOPTYSIS

To the Editor:—*What is the rationale in applying ice bags to the chest in persons with tuberculosis who are having hemoptysis? These people are usually quite ill, and it seems this treatment only causes worse physical and mental distress and does no good.* *T. R. Pratt, M.D., Pismo Beach, Calif.*

Answer.—Ice bags were long applied to the chest of tuberculous persons during and immediately after pulmonary hemorrhage. This procedure was never on a rational basis. In 1922, Fishberg said, "The time-honored ice bag applied to the chest is of no value at all excepting to keep the patient busy and attentive while attempting to keep it in place." From about 1 to 3% of pulmonary hemorrhages have proved fatal because of profuse bleeding resulting in cerebral anemia or to aspiration of blood in sufficient quantity to cause suffocation. Usually these are sudden deaths. However, the great majority of hemorrhages come under control without immediate complication with or without the use of ice bags. Thus, any useless procedure could be introduced and extravagant claims made for it. It is not unusual for small to moderate amounts of blood to be aspirated into bronchial ramifications during hemorrhage. These, together with surrounding reaction, cast shadows on x-ray films, which may be in evidence for weeks or longer. In some such cases, pneumonia develops in such areas. It is believed the ice bag may invite the development of pneumonia. The ice bag should be classified as an anachronism in the sense that it is being used long after it was found to be of no value and, possibly, harmful. In cases of persistent, extensive bleeding, artificial pneumothorax has been successfully used. When this is impossible because of adhesions, surgical resection may become necessary.

TREATMENT OF SYPHILIS AND PENICILLIN SENSITIVITY

To the Editor:—*What therapeutic procedure should be followed in cases of cerebrospinal syphilis in which the process is active and a penicillin sensitivity has developed? Specifically, what would be the procedure in cases showing an anaphylactic reaction and those showing apparently minor skin reactions? It is understood that the reactions mentioned are associated with old syphilis and not with recent infections.*

R. L. Nattkemper, M.D., Napa, Calif.

Answer.—In the treatment of cerebrospinal syphilis, when a penicillin sensitivity has developed, treatment with that drug should be immediately and permanently discontinued. This applies particularly to anaphylactic reactions but should also apply to minor skin reactions, since the latter may be prodromal to more severe reactions from which a fatality could occur. However, other antibiotics may be employed and are preferable to arsenicals such as oxophenarsine hydrochloride hemialcoholate (Mapharsen) or neoarsphenamine. In the order of choice, oxytetracycline (Terramycin), chlortetracycline (Aureomycin), tetracycline (Achromycin), or chloramphenicol (Chloromycetin) are all to be considered. The usual average dosage is 2 to 4 gm. daily, in divided dosage, usually continued if tolerated for four weeks.

PREPUBERAL BREAST PAIN

To the Editor:—*An 11-year-old girl complains of pain in nipples, areolas, and breasts. There is no evidence of trauma, tumor, infections, or congenital defects. What factors may be present to cause the pain? How frequently does pain occur in the prepuberal period? What is the suggested treatment?*

Joseph V. Waitkunas, M.D., Woodhull, Ill.

Answer.—Pain in the nipples and breasts is an infrequent symptom in girls of prepuberal age. However, the condition such as you refer to has been described in some of the older works on diseases of the breast. Pain may be due to trauma of the nipple, which may not be evident on examination, such as from pinching, squeezing, or other forms of traumatic nipple stimulation; even the possibility of foreign body, such as needles inserted into the nipple ducts, must be considered. The condition is much more likely to be what older works on the subject call "the hysterical breast." This was known as early as 1667, when it was described by Willis, and is characterized by pain, tenderness and swelling of the breast, and reluctance on the part of the patient to submit to examination. When a diagnosis has been established, and the possibility of foreign body has been eliminated (x-ray examination if necessary), a frank discussion with the patient, with the assurance that there is no actual disease or tumor growth present, is usually sufficient. The patient should not receive hormones or physical therapy, but psychotherapy may become necessary.

TETRACYCLINE AS A FOOD PRESERVATIVE

To the Editor:—*With a chicken bought recently was a statement that tetracycline had been used as a preservative. Is there any danger of either sensitizing people to this drug or creating a resistant bacteria that would not respond to later medication with this drug? If this is successful in reducing spoilage in fowl and fish, is there not a danger that this food will be left too long on open shelves?*

Walter B. Cox, M.D., Missoula, Mont.

Answer.—Since Nov. 23, 1955, it has been permissible to use chlortetracycline for the preservation of freshness in dressed poultry. Chlortetracycline is usually added to the mixture of ice and water in which chickens are cooled after evisceration in poultry processing plants. A tolerance level of 7 ppm for residues of chlortetracycline in or on uncooked poultry has been established. Experimental evidence has shown that cooking destroys the antibiotic. Theoretically, therefore, the consumer is not exposed to antibiotic activity. The question of sensitization of a large human population was given serious consideration prior to the establishment of the tolerance level in uncooked poultry. Chlortetracycline is being widely used in the commercial fishing industry to assist in the shipboard preservation of the catch. Experimental work with other antibiotics in food preservation is in progress. The retailer is interested in what he calls the extension of shelf life of perishable products. Chickens and fish properly treated with chlortetracycline do have a longer shelf life. The retailer must assume the same responsibility as previously with respect to sanitation and edibility of a product. Antibiotics reduce, not prevent, spoilage, and vigilance must be exercised to guarantee safety of all perishables.

ALLERGENIC EFFECT OF PENICILLIN

To the Editor:—*In preparing a solution of penicillin for sensitivity skin testing, may the solution be kept indefinitely and still be reliable as a test solution? Does outdating of the penicillin affect its reliability as an ingredient of the test solution?*

M.D., West Virginia.

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—There is good evidence that the allergenic activity of penicillin solutions is far more stable than its antibiotic property. Penicillin moderately "outdated" is probably still potent allergenically. Weak solutions of penicillin have been kept for a long time, with little impairment of its allergenic qualities. It is very unlikely that such solutions can be kept active "indefinitely." It is not known exactly for how long they remain active.

Answer.—Solutions of penicillin to be used for sensitivity determination by skin testing are best made up fresh. If penicillin is allowed to stand in solution for any appreciable length of time, it may deteriorate. Penicillic acid may be split off from the molecule, and the antigenic capacity of the antibiotic will probably be lost. If solutions of the antibiotic are to be kept for any length of time before they are to be used for skin testing, they are best kept in the frozen state. Outdating of penicillin does not impair its reliability as an ingredient of the test solution, providing the powder has been kept dry.

COLD SHOWERS AND ALLERGY

To the Editor:—*A 68-year-old man has been allergic most of his life to many inhalants, some foods, and currents of air contacting his scalp. The first two classes of allergens affect him periodically. The air currents produce coryza and nasal congestion any time he exposes his uncovered head to a draft of air. In an attempt to desensitize his scalp against air currents, he began to take cold showers in the mornings, five months ago, with no apparent effect. His general physical condition is fair. He works about 10 hours a day and has no time for hobbies or physical exercise. For the past four years, walking up steps has caused dyspnea. His pulse misses a beat irregularly, and chest x-ray shows moderate atherosclerosis of the aorta. Blood and urine are normal. Is there any hazard for him in cold showers?*

M.D., California.

Answer.—The history of this man suggests that the allergy to the inhalants is probably the primary condition. It is not uncommon for persons having a true allergy to experience acute reactions to physical stimuli, particularly to cold, dampness, and drafts. There are, of course, true instances of primary hypersensitivity to cold. Attention to the basic allergy in this patient might prove more profitable than any attempts to modify the physical hypersensitivity. If this proves unsuccessful, cold showers are worth trying. The history does not indicate any particular reasons for considering cold showers hazardous to this patient.

COUGH AND PAIN MEDICATION DURING PREGNANCY

To the Editor:—*What cough medicines and pain-relieving drugs can be administered to a pregnant woman without doing any harm to the fetus and without provoking abortion? What are the safer doses, taking into consideration especially such drugs as morphine, codeine, Dionin, phenobarbital, and papaverine?*

M.D., Turkey.

Answer.—The safe cough medicines and pain-relieving drugs used in nonpregnant patients may be administered to a pregnant woman without fear of harming the mother or inducing an abortion. The doses are the same for pregnant as for nonpregnant patients.

OLEANDER AND DECOMPENSATED HEART DISEASE

To the Editor:—*A patient with decompensated coronary heart disease is allergic to both digitalis and squill. Would oleander compound be of value and, if so, what company in the United States manufactures it?*

Harry R. Deane, M.D., St. Petersburg, Fla.

Answer.—Nerium oleander is a plant of the Apocynacea family, many of which contain glycosides with a digitalis-like action. Strophanthus is a member of this family. The active principle of oleander, oleandrin, becomes gitoxigenin on hydrolysis. This material is also the result of hydrolysis of gitoxin, one of the so-called pure glycosides of digitalis. With this background it seems likely that a patient who was allergic to all of the digitalis glycosides would also be allergic to the glycosides of oleander. Oleander disappeared from medical practice in the United States many years ago, although reports in the foreign literature indicate that it is used, but rarely, on the European continent. Inquiries at three large urban pharmacies failed to discover a preparation of oleander or to elicit information as to where such a preparation might be found. There are four purified glycosides of digitalis readily available today in any pharmacy. In additon there are strophanthin and ouabain. It would seem reasonable to suppose that one of these preparations would prove effective in the above instance without producing undesirable side-effects.

PERFORATIONS OF TYMPANUM

To the Editor:—*In 1952, I was struck by lightning while deep-sea fishing and sustained a basilar skull fracture and ruptured both tympanums. The residual is nonserviceable hearing in the left ear with an open tympanum and 60% loss of hearing in the right ear with a healed intact tympanum. At times I am exposed to a water hazard in which there is possibility that my head might be submerged momentarily under water. I should like information as to an appliance or, if necessary, an operation, if the latter could seal off my middle ear. Obviously, I would prefer an appliance, if such exists, that will answer the problem—even for exposure to accidental pressures, say at a depth of 10 to 15 ft. of water.* M.D., *New York.*

Answer.—Closure of long-standing tympanic membrane perforations is an accepted procedure. One method recently described by E. L. Derlacki (Repair of Central Perforations of Tympanic Membrane, *A. M. A. Arch. Otolaryng.* 58:405 [Oct.] 1953) consists of a series of office treatments and is successful in better than half of the cases, even when the perforation involves a large portion of the tympanic membrane, provided there is an intact margin. More recently methods of closing perforations by surgery have been described in the foreign and American literature. Meanwhile occlusion of the meatus with lamb's wool to which petroleum jelly has been applied generally secures a water-tight protection against immersion.

DERMATITIS FROM CHLORINE

To the Editor:—*A patient has extensive dermatitis of the hands that seems to clear up when she moves to an area with an unchlorinated water supply. Hypochlorites and other chlorine bleaching compounds make the dermatitis definitely worse. However, this woman now lives in an area in which the municipal supply is chlorinated. Is there any way to counteract the chlorine in the water?*

Everett C. Campbell, M.D., Woodsville, N. H.

Answer.—There is no known simple and practical way of removing free chlorine from municipal water supplies other than by boiling or by allowing the water to stand overnight in containers with maximum surface exposure to the air (tubs, dishpans, etc., rather than bottles). These methods will serve to remove free chlorine but will not remove chlorinated derivatives that may also be present in such water and that have been claimed to be capable of producing allergic reactions in sensitive individuals. Perhaps the use of protective creams, such as those containing silicones (New and Nonofficial Remedies, 1956, p. 479), might be tried, since it would hardly be feasible to employ distilled water for dishwashing, laundering, and other household uses.

FLYING AFTER OCCURRENCE OF PNEUMOTHORAX

To the Editor:—*A 28-year-old male has just had his second spontaneous pneumothorax in three years. The first occurred while he was in military service and it was presumed to be due to a bleb; the etiology of the present episode is undetermined. This man holds a private pilot's license for small planes. From this information, can it be stated whether he should fly after recovery, and, if so, would there be any altitude limitations?*

F. H. McClain Jr., M.D., Mount Union, Pa.

Answer.—The history of two episodes of spontaneous pneumothorax within a three-year period indicates that this individual is a good candidate for repetition of the incident. He, therefore, represents a poor risk as a flyer, in that he compromises flying safety. Whether a bleb was actually proved in the first episode is not obvious in the question as stated. It would be advisable to study the case thoroughly, including laminograms. If blebs are identified and are on the same side as the pneumothorax, surgical removal of the pathology may rehabilitate this man and permit flying. However, recovery must be complete after surgery, including a return to normal pulmonary function.

COOKING WITH MINERAL OIL

To the Editor:—*Is there evidence that cooking with mineral oil results in the formation of carcinogenic agents from oil decomposition?*

Daniel J. Reagan, M.D., Worcester, Mass.

Answer.—There is no conclusive evidence indicating that mineral oil, when used in cooking, is decomposed to form carcinogenic substances. The use of mineral oil in cooking is not a desirable practice; it is well known that the ingestion of mineral oil interferes seriously with bodily absorption of the fat-soluble vitamins carotene, vitamin D, and vitamin K.

HAZARDS IN USING OXYGEN TENT

To the Editor:—The Journal, *June 30, 1956, page 934, in the answer to a query entitled "Hazards in Using Oxygen Tent," contains the extraordinary statement that a spark of static electricity could start a conflagration in an oxygen tent under certain circumstances, such as the use of nylon in any form, sheets or bedclothes, as well as the use of wool blankets. We do not believe there is any evidence to support such a contention. It is of considerable importance to question the authority of the consultant to answer the query, not only from the point of view of fact and theory but also because a medicolegal basis for suit would exist when a fire did occur during the use of an oxygen tent. We have never been able to start a fire with deliberately produced static sparks on wool blankets in atmospheres of 40 to 50% oxygen. Our studies were made in oxygen chambers many years ago to test this point. Since confusion exists regarding the hazard of fire in the presence of oxygen as contrasted to that in the presence of flammable or explosive gas atmospheres as found in operating rooms, the following discussion is presented.*

For a fire to start under any conditions two factors are necessary: (1) a flammable or explosive material and (2) a source of heat sufficient to raise the temperature of the material above the kindling point. Certain anesthesia gases are flammable and have a very low kindling or flash point; hence a static spark may ignite them very easily. In contrast, oxygen is not flammable; it only supports combustion. For a fire to start in an oxygen atmosphere it is necessary that the flammable material in the oxygen atmosphere start burning. The kindling point of cotton sheets or wool or nylon blankets is considerably higher than that of the afore-mentioned anesthesia gases; hence it is much more difficult to ignite them. The presence of greater or lesser amounts of oxygen does not affect the kindling point of the material mentioned.

A static spark obtained from wool blankets or nylon uniforms has sufficient heat and intensity to raise the temperature of explosive gases above the kindling or flash point. It cannot, however, do this with bedclothes, etc. Therefore, there is no danger of fire from this source in oxygen atmospheres. While static sparks do not create a hazard in oxygen tents and in rooms, the presence of electrical appliances, any of which may "short" or spark, does. Electrical appliances and open flames should be rigidly excluded. We have been advised by the Linde Air Products Company that their Safety Codes Division, which has kept accurate records of practically all oxygen fires in the United States during the past 25 years, finds that about 90% of these fires have been caused by smoking. They further state that, of the remaining 10%, some were probably caused by smoking, although the evidence for this belief could not be definitely obtained. Other sundry causes have been open flames from alcohol lamps placed in tents, sparks from electrical appliances, and burning candles.

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The above letter was referred to the consultant who answered the Query and Minor Note under discussion. His reply read as follows:

> *I agree with the writers that ordinarily a spark of static electricity would not cause a fire in an atmosphere of 40 to 50% oxygen. Experimentally one might attempt it 1,000 times with negative results, but on the 1,001th try have a positive result. One must not overlook the fact that patients expel intestinal gases and exhale anesthetic gases during recovery from anesthesia. There is always the possibility of low combustion point of foreign material having been spilled on bedding under the tent. The National Fire Protective Association's "Standard for Nonflammable Medical Gas Systems," which has been adapted by the National Board of Fire Underwriters, specifically prohibits wool blankets and nylon fabrics within an oxygen tent. This was approved, along with other rules, by the Committee on Hospital Operating Rooms and the Committee on Gases, both of which are made up of outstanding experts on this subject. The majority of oxygen tent fires have been shown to result from persons smoking under the tent, but some have not been explained. This, therefore, is no argument against the possibility of static causing a fire.*

TREATMENT OF TRICHURIASIS

To THE EDITOR:—*In Queries and Minor Notes in* THE JOURNAL, *Aug. 25, 1956, page 1719, there is a treatment for trichuriasis. I should like to comment on this subject. Light infestations by Trichuris trichiura (one or two eggs per preparation for direct examination) do not require treatment, because the number of parasites is so small that no ill-effects are produced in their host. Heavier infestation may be treated with enemas of 1:300 colloidal hexylresorcinol carried to the cecum. To date, no other treatment has been found equally effective. To assure success, these enemas must be carried to the cecum, preferably under fluoroscopic control. The evening before and two hours before giving the medicamentous enema, the patient must receive a cleansing enema with a 2% solution of salt in warm water.*

The medicamentous enema must be prepared as follows: hexylresorcinol, 3 gm.; mucilage of acacia, 90 gm.; barium sulfate, 90 gm.; and warm water, quantum sufficit, 900 cc. Generally, to fill the colon up to the cecum, adults need 1,000 to 1,500 cc. and children 15 to 20 cc. per pound of weight, or 100 to 150 cc. per year of apparent age. The enema may be evacuated 5 to 10 minutes after administration. Children frequently retain about a third of the amount used. Some cases are cured with the first enema; others require three or more enemas. These must be given at weekly intervals. Two weeks must elapse after the last enema, to allow for a new examination of feces. It must be stressed that the destructive action of colloidal hexylresorcinol, 1:300 solution, is so strong that the intestine becomes rid of Trichuris (Trichocephalus) organisms up to the level reached. Some patients have expelled over 2,000 Trichuris organisms after the first enema. The worms come out in pieces or almost totally disintegrated.

Trichuriasis is very common in Cuba. In this country, the dysenteric syndrome produced by the Trichuris organisms in children is more frequent than the one caused by Endamoeba histolytica or Balantidium coli. The differential diagnosis is easy, by means of scraping of the margins of the anus with a sterile cotton swab; microscopical examination will show, according to the case, Trichuris eggs (free or englobed in flocculi of mucus) or trophozoites and cysts of histolytica, or B. coli. A rectoscopic examination is valuable to establish diagnosis, because in children T. trichiura is found very often in the rectum-sigmoid (rectal trichuriasis). It is common to find rectal prolapse showing a reddish, edematous mucosa with small ulcerations and numerous Trichuris organisms adhered to it.

If the dysenteric syndrome produced by T. trichiura is not stopped quickly, the patient may die of gastroenteritis and dehydration in a few days. In cases of rectal trichuriasis with dysenteric syndrome, these enemas must be applied with no previous preparation (cleansing enemas). After the first enema the number of evacuations diminishes noticeably, and the stools become normally consistent and without macroscopic blood. Seventy-two hours later, the alarming clinical picture is almost completely vanished, and the patient recovers rapidly, clinically and parasitologically.

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ARMY PERSONNEL "GASSED" DURING WORLD WAR I

To THE EDITOR:—*In Queries and Minor Notes, in* THE JOURNAL, *Aug. 18, 1956, page 1604, Dr. W. C. Hueper mentioned Case and Lea's report "Mustard Gas Poisoning, Chronic Bronchitis, and Lung Cancer"* (Brit. J. Prev. & Social Med. *9:62, 1955). It should be mentioned that, according to these British authors, over 80% of surviving World War I pensioners who suffered from mustard gas poisoning were affected by chronic bronchitis some 15 years later. This seems to indicate that, contrary to the answer given to the original query* (J. A. M. A. *161:118 [May 5] 1956), the majority of "gassed" veterans do have residuals from their exposure to mustard gas. Dr. Hueper also mentioned that a statistically significant excessive liability to lung cancer was found in British veterans with mustard gas poisoning. However, he failed to add that, in the same study, a similar excess of lung cancer was found also in those veterans of World War I with chronic bronchitis who had never been exposed to mustard gas. Therefore, Case and Lea concluded that the evidence presented "does not support the view that mustard gas has acted as a direct carcinogen" but indicates that chronic bronchitis may be associated with the subsequent development of pulmonary malignancy. Bolt and Lew* (J. A. M. A. *160:736 [March 3] 1956) also demonstrated that chronic bronchitis of any etiology increases significantly the risk of death from respiratory cancer. Indeed, more and more pathological and clinical investigations, most of them conducted abroad, indicate that pulmonary malignancy may be a late sequela to profound chronic and scarring processes in the lungs, be they initiated by chemical or mechanical injuries, epidemic influenza, or tuberculosis (Finke:* Internat. Rec. Med. *169:61, 1956).*

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SCHIZOPHRENIA

To THE EDITOR:—*In* THE JOURNAL, *Sept. 8, 1956, page 152, in Queries and Minor Notes, it is stated that "in cases of schizophrenia, for 'patients who are moody, nontalkative, and depressed and who have been mentally ill for many years,' the ideal treatment should be a combined convulsive and insulin hypoglycemic treatment. . . . [but] even with this most energetic form of treatment, one cannot assume more than about 15 to 20% probability of a favorable response."*

It seems to me that where the consultant's "ideal treatment" offers no more than a 15 to 20% cure, other possible forms of therapy should at least be mentioned. In recent years, some psychotherapists have been treating even chronic schizophrenia with modified psychoanalytic techniques. This is at best a difficult, specialized therapy, still in its investigative and developmental stages, with many variations from therapist to therapist, and for which few statistics are available; but such results as have been published and my own experience would indicate as good, or better, expectations than the 15 to 20% with combined convulsive and insulin treatment. Incidentally, the consultant also makes no response to the query about "serious side-effects"; there is, of course, significant hazard and mortality connected with the recommended treatment. Further, in the present state of our psychiatric nosology, it seems ill-advised categorically to recommend a hazardous, relatively ineffectual therapy, simply because a patient has been sketchily described as "moody, nontalkative, depressed," and schizophrenic.

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« Washington News »

25 State Society Medicare Contracts Signed • •
Library of Medicine Surveys Dissertation Use • •
More Public Health Service Assignments Shifted • •
Health Conditions of Indians • •
Loans to Medical Schools • •

MEDICARE CONTRACTS

The Defense Department and medical societies that will serve as agents for the provision of medical care outside military facilities for armed forces dependents are moving rapidly toward a conclusion of negotiations. The contracts are expected to be completed with the societies in time for inauguration of the program Dec. 7. Approximately a month before the deadline, 25 societies either had formally signed contracts or had completed negotiations with the Defense Department. Contracts formally signed were with medical societies of Colorado, Washington, Indiana, Oregon, Montana, and Nebraska.

The department said there were no problems serious enough to interfere with formal signing of agreements covering California, Minnesota, Michigan, Wisconsin, North Dakota, North Carolina, Connecticut, Massachusetts, New Jersey, New Hampshire, Vermont, South Dakota, Illinois, Florida, Tennessee, Arkansas, Oklahoma, Wyoming, and Iowa. The Army is the agent for all uniformed services in handing medicare, with operations handled by the Office for Dependent Medical Care, headed by Major Gen. Paul I. Robinson.

SURVEY OF USE OF DOCTORAL DISSERTATIONS

The National Library of Medicine has made a survey on the use of its collection of doctoral dissertations in medicine. It found that the number of these requested per week averaged 19, compared with 35 several years ago, and that the largest number requested were from readers in the library itself, 38% as against 24% for interlibrary loan. Of the 44 universities whose theses were requested, 10 schools account for 64% of all requests.

In reporting on the survey, the library commented: "While it takes pride in its stewardship of the theses collection, the library has occasionally felt it necessary to evaluate the effort put into acquiring, processing, housing and servicing it. In the past few years, especially when space has been at a premium, the question of the considerable shelving which must be used to store the new and also the old theses has come up again and again with various solutions advanced each time. Basically, the position of the library is that if theses are valuable for medical knowledge, the necessary time, money and effort will be found and expended on them, otherwise not. But the value of a medical work is extremely difficult to measure and, like the value of circulating iodine in the thyroid, must be sought for indirectly. One such indirect method of determining the value of material in a library is by examining the frequency of its use." There still remain some unanswered questions, the library adds in a report in its monthly publication, before intelligent decisions can be made about the theses collection.

REASSIGNMENTS IN PUBLIC HEALTH SERVICE

More reassignments in the Public Health Service have been announced in the wake of the major shifts made several weeks ago by Surgeon General Leroy E. Burney. Dr. Donald W. Patrick, director of the 500-bed Clinical Center at Bethesda, Md., has been appointed medical officer in charge of the 541-bed PHS hospital at San Francisco. Dr. Patrick succeeds Dr. Kenneth R. Nelson, who comes to Washington as associate chief of the Bureau of Medical Services.

Dr. Nelson, in turn, fills the post left vacant by Dr. G. Halsey Hunt's appointment as director of a new Center for Research on Aging, to be set up at the National Institutes of Health. Dr. Patrick's post at the Clinical Center has been filled by Dr. Jack Masur, former chief of the Bureau of Medical Services. That bureau is now headed by Dr. John W. Cronin, former director of the PHS Hill-Burton hospital construction program. The bureau supervises PHS hospitals, the Hill-Burton program, Indian health programs, and the foreign quarantine service. In another shift, Dr. Burney appointed Dr. Edgar B. Johnwick as medical officer in charge of the National Leprosarium at Carville, La. He succeeds Dr. Eddie M. Gordon, newly appointed chief quarantine officer at Fort Monroe, Va.

HEALTH CONDITIONS AMONG AMERICAN INDIANS

In a question and answer booklet, the Department of the Interior's Bureau of Indian Affairs describes the conditions and problems of the American Indians in health, housing, and other matters. For more than a year, the Indians' health has been the responsibility of the U. S. Public Health Service, but the Bureau of Indian Affairs retains responsibility in other respects. The booklet points out the role of the PHS and notes that costs of Indian medical care are met through annual congressional appropriations. In health matters, the bureau says, the objectives are "to bring the health of the Indians to the level enjoyed by the rest of the population in a way that encourages self-reliance and

(Continued on page 54)

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Washington News—Continued

independence and gives full recognition to their rights as citizens. This requires adapting the health program to the customs, traditions, temperament and culture of each tribe."

Health work is described as a cooperative effort between the PHS, the Bureau, tribal organizations, and the individual family members. "Tribal councils usually include committees on health," the report states, "and these committees work cooperatively with public health officials." Many Indians trained as practical nurses and sanitary aides are helping their own people, while employed by the PHS. Also at work on the reservations are some Indians who have medical degrees or nurses training. Other points in the booklet are as follows:

Some tribes completely support their own health facilities, with the full cooperation of the PHS.

The PHS provides direct medical care as well as public health services for disease prevention. Hospitals, sanatoriums, health centers, field clinics, and school infirmaries cooperate, and some Indians are cared for in private facilities at federal expense. In some cases state health departments assist.

To improve Indians' health conditions, the PHS has expanded the quality of curative medical care and at the same time has intensified its program to prevent disease through field health facilities and services, immunizations, case finding, public health nursing activities, maternal and child care, school health, sanitation, health education and dental public health, and curative services. Public health services are furnished without charge, but Indians financially able to do so are expected to pay for medical, hospital, and dental care according to a schedule established by the PHS.

Although originally it appears that Indians and non-Indian settlers were "on about equal terms healthwise," today Indians fall victim to more infectious and preventable conditions, attributable to the "present low standard of living among the Indians."

Although the tuberculosis rate for Indians is far greater than that for the rest of the population (12 times in 1954), progress is being made through x-rays, surgery, occupational therapy, inoculations, antibiotics, and general rehabilitation.

LOANS TO MEDICAL SCHOOLS

The 12th loan to a medical school for construction of dormitory facilities has been made by the Community Facilities Administration (CFA), an affiliate of the Housing and Home Finance Agency. The CFA announced a $1,100,000 loan to Indiana University Medical School for a dormitory addition. Since the program began in 1950, the agency has loaned about 500 million dollars to institutions of higher learning for such improvements as dormitories, dining rooms, student unions, and infirmaries. Of this total some 14 million dollars has gone to 12 medical schools.

Money is loaned for a 40-year period at 2⅞% interest. Criteria for a loan include the following requirements: 1. The institution must offer a two-year program acceptable for full credit toward a baccalaureate degree. 2. The school must be nonprofit. 3. Additions or new construction must not be of extravagant or elaborate design. 4. Construction excludes class rooms, gymnasiums, or stadiums. When Congress voted the program it approved 300 million dollars in loan authority; this was raised to 500 million dollars in 1955 and to 750 million dollars this year. Applications for loans are available at the six regional offices of the housing agency, at New York, Philadelphia, Atlanta, Chicago, Fort Worth, Texas, and San Francisco.

SURVEY OF NURSING HOMES AND GENERAL HOSPITALS

A nationwide survey of the geographical distribution of nursing homes and general hospitals providing skilled nursing service has been completed by the Public Health Service The report includes 564,826 beds in 5,200 general hospitals and 171,106 beds in 6,531 skilled nursing homes. Patterns of the study reveal that in metropolitan counties there are approximately 4.1 general hospital beds and 1.3 beds in skilled nursing homes for every 1,000 population, while isolated rural counties have 1.8 hospital beds and 0 4 beds in nursing homes for 1,000 The supply of beds tends to increase in proportion to the per capita income and the number of doctors and nurses. Beds in nursing homes increase in accordance with the number of persons aged 65 or older. The complete study was published as Public Health Monograph No. 44, and the patterns are discussed by Jerry Solon and Anna Mae Baney in the October *Public Health Reports.*

DIABETES PROGRAM GUIDE

The Department of Health, Education, and Welfare has published a Diabetes Program Guide to aid states in improving their public health work in this area. The first part of the booklet discusses briefly the groups that might cooperate in conducting a diabetes program, the educational channels that could be used, and the various sectors of the population that would profit most from the program. However, as these factors vary from community to community, the high point of the pamphlet is the detailed outline of diabetes tests, equipment and personnel needed, and costs. The appendix suggests record forms and letter forms. This information provides a concrete basis for planning and conducting a control program. Nationwide use of diabetes control would prevent the occurrence and progression of the disease and would contribute to the scientific knowledge of the disease.

MISCELLANY

The steady expansion of activities for children and the changes in a child's life in the 20th century are reviewed in a new history of the Children's Bureau, "Four Decades of Action for Children." . . . The United States Air Force Medical Service consultants will visit various U. S. A. F. medical installations in Europe and will attend a medical conference in Germany this month. . . . The Atomic Energy Commission announced that the auxiliary monitoring system operated by the Public Health Service has been discontinued. The monitoring system informs the public of the levels of radioactivity in the U. S However, the AEC continues its own around-the-clock monitoring. . . . The PHS is ready to act on grant applications for aid in building sewage treatment facilities.

(cont'd)

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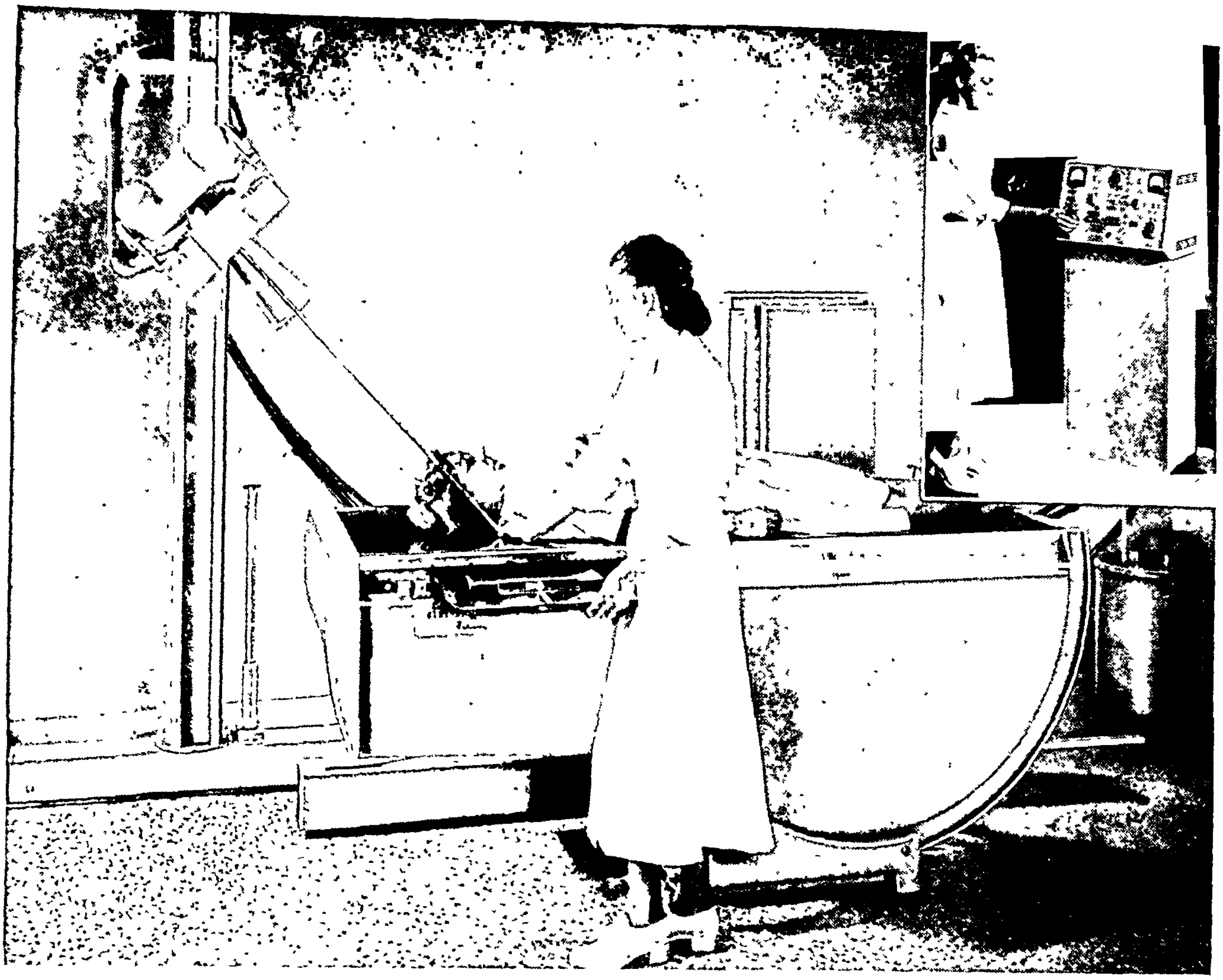

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THE JOURNAL

of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 162, NO. 12 — CHICAGO, ILLINOIS — NOVEMBER 17, 1956

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THE OLYMPIC GAMES AND THE OLYMPIC IDEAL

Allan J. Ryan, M.D., Meriden, Conn.

• *The Olympic Games are of such a personal nature to the world that they can even override serious political differences between countries. Here is presented how athletic training, the forerunner of the games, had its beginning. In considering the trials and tribulations that befell the growth of gymnastic exercise, it will be seen that physicians are involved not only in the etiology but almost as equally as competitors in the actual contests. New organizations, such as the American College of Sports Medicine, assure greater participation by the medical profession in future athletic affairs.*

This year more than 70 nations will send representatives to Melbourne, Australia, to compete between Nov. 22 and Dec. 8 in the 11th Olympiad. Competition has already been completed in the seventh Winter Games at Cortina, Italy, and in the equestrian events held in June in Sweden, because of the six-month quarantine on horses required by Australia. Sixty-nine nations, a record number, sent competitors to Helsinki, Finland, in 1952. What is the nature of these contests, which draw the attention and participation of men and women from all over the world every four years and which can override serious and fundamental political differences to the extent that East and West Germany can unite to send a single team? How are they related to the ancient Olympic Games of Greece, and what is their sponsorship? Why should physicians be interested in these demonstrations of skill, strength, agility, and endurance?

Probably the most ancient of all sports is hunting. Although we have pictorial records of the practice of this activity from the ancient Egyptian and various Asiatic nations and fragmentary records of other competitive activities, we do not consider that these people looked upon these endeavors as sport in the modern sense. The early Irish tribes held their Tailtean games in the pre-Christian era, but our knowledge of this time is so obscured by mythology that we do not have a clear idea of these contests. The ancient series of Olympic Games held on the plains of Olympia in Greece are well documented from the year 776 B.C. until they were abolished by the Emperor Theodosius in 394 A.D. These games, therefore, for practical purposes, mark the beginning of the recorded history of athletics.

We do not know the exact reason for the introduction of the competitive foot race, which marked the first Olympic contest, into the religious festivals that had been celebrated on these plains probably for hundreds of years before that. We do know that, although the games were originated by the Eleans who were the inhabitants of that region, they soon shared control of the games with the Spartans, even when these two states were at war. During such times a "truce of the gods" was zealously observed for the period of the games. We should also realize that, during their thousand-year history, these games bequeathed to us not only a series of contests, many of which are practiced and enjoyed today, but also the ideal of amateurism in athletics, which is the basis of the widespread interest and participation in sports today. In fact, the games were eventually abolished, because they had become so corrupted by the gradual inroads of professionalism that they had lost their true character and inspirational force. The first recorded Olympic game consisted of a single contest. a foot race the length of the stadium, which we know was about 200 yd. long. It was won by Coroebus, who was by profession a cook. A monopoly of victories by the hosts was maintained until the 13th Olympic Games, when the first non-Elean was returned a victor. At the 14th games, a second race, twice the length of the stadium, was added, and at the 15th a still longer race. The 18th Olympics saw the introduction of the pentathlon, due to the influence of the Spartans. This was at first an elimination contest in which the competitors were gradually narrowed down as they progressed through the broad jump, javelin throw, foot race, and discus throw. The two best then wrestled for the championship.

Boxing was added to the program at the 23rd games, the four-horse chariot race at the 25th, and the pancratium (a very rough combination of boxing and wrestling) at the 33rd games. Gradually contests in art, sculpture, and music were also added. In fact, the term athlete originally applied to one who competed for a prize in the games, whether in musical, gymnastic, equestrian, or other competition. By the 77th Olympiad, the games lasted for five days and included two lengthy religious ceremonies. For the first time representatives of all countries bordering on the Mediterranean were invited. It was indicative of the international character of the games that the final victor at the last games in 394 A.D. was Varastad, an Armenian.

History of Athletic Training

Those who competed at the Olympic Games were expected to spend 10 months in hard preliminary training. As the number of events increased and competition became wider and keener, those without a considerable or independent income found it hard to devote the necessary time to training. At the site of the games, training table meals were provided. Fried and boiled foods and cold drinks were forbidden. Cheese, figs, and wheat bread were staples of the training diet. Most of the competitors abstained totally from wine during training periods. Only light conversation was permitted at meal times to encourage proper digestion. Women were never allowed to compete, and at first were not even allowed to witness the games. This prohibition was eventually disregarded after a mother came disguised as a man to see her son compete. The prescribed penalty of being hurled from a high rock was not invoked in her case, and thereafter women were gradually admitted as spectators. There was an upper age limit of 35 for all contestants. In later games, separate contests for boys and youths were arranged. All athletes competed without clothing and their bodies were salved with oil. This practice probably had more of a ritual than a practical significance, although it must have made the wrestling contests difficult.

Professional athletics, which was to prove the downfall of the games eventually, began in Greece about the fifth century B.C. During the early Roman empire, amateur athletes were virtually unknown. Moreover, professional athletes finally supplanted the gladiators, who were principally prisoners or slaves, in the public circuses. The professionals were mostly Greeks and were organized in guilds. The ancient philosophers and physicians were unanimous in condemning the profession of athletics as injurious to the mind and body.

In medieval times the nobility found their exercise in training themselves in the strenuous art of war, which involved principally hand-to-hand combat on foot or horseback. They practiced hunting for diversion as well as to supply the larder. The common people had their own games, such as throwing the stone, a type of football, and quarter-staff. Gymnastics survived principally in the families of professional acrobats who entertained the nobility. Edward III of England prohibited weight-throwing by statute, but Henry VIII tossed the heavy pole, threw the hammer, and pole-vaulted. He also excelled at the game that eventually became court tennis, which was played first in the dry moats of the French castles.

Italian physicians of the Renaissance revived interest in gymnastic exercise for therapeutic purposes. Little general attention was paid to this subject, however, until the early 19th century. F. L. Jahn, a Prussian, devised a series of exercises for his Turnhalle gymnasium with the specific object of fitting German youth to rise above Napoleonic domination. The battles of Leipzig and Waterloo came too soon after he had begun this self-imposed mission, however, for his work to have had much influence. In Sweden, Per Henrik Ling (1776-1839) added to and modified the classical exercises to produce the routine that we know as Swedish gymnastics today. Gymnastics was first taught in America in 1825 by Charles Follen and Charles Beck, who were pupils of Jahn. Dio Lewis created a vogue for light exercise with rings, dumbbells, and bar bells between 1860 and 1870. In 1879 the Hemenway gymnasium opened at Harvard with Dudley Sargent's apparatus, and in 1889 Nils Posse introduced the Swedish system of gymnastics to this country and the Boston Normal School of Gymnastics was founded. The integration of gymnastics into the educational program was signalized by the first appearance of the term "physical education" in 1880. The International Gymnastic Federation with representation from Europe and the United States was founded in 1881, but it was not until 1923 that a complementary federation of educative gymnastics was organized. This may have been due to the fact that in France and Germany physical training by gymnastics remained under state control.

Rebirth of Olympic Games

During the 19th century, regularly scheduled athletic and gymnastic meetings began to appear. The German Turnvereine derived from the Turnhalle gymnasium of Jahn. The first regularly organized athletic meeting of modern times in England was held at the Royal Military Academy in Woolrich in 1849. Organized meetings and the growth of athletic clubs called for larger federations to regulate them. The Amateur Athletic Union was formed in the United States in 1888, eventually creating order out of chaos. This association established the pattern for the modern Olympic organization.

The man who was responsible for the modern revival of the Olympic Games in 1896, Pierre de Coubertin of France, was not an athlete himself and had no particular interest in the effect of athletics on the development of physique. He conceived of the idea of the games as a revolution in education that would employ sport as a medium. As a young man he had pondered the question as to why the small island of England could produce leaders who could and did dominate such a large area of the world, producing such tremendous wealth and influence for the mother country. He thought that he found the answer in the English public school system, which recreated the adult world in miniature with its own class system, the struggles and injustices, and the great emphasis on athletics as part of the curriculum. If only, he thought, every country in the world could have the incentive to train its youth in the keen struggle of international athletic competition, the same success might result in the development of their characters. Perhaps we might call this a sort of preventive psychosomatic medicine.

Many have since argued that the games should be discontinued because the disputes with which they are frequently marred are not conducive to international amity. It was never the intention of the founder that they should be. In London over 40 years ago Coubertin made the following statement after a particularly violent series of incidents in the 1908 Olympic Games:

> Heaven preserve us from a society in which there are no excesses and where any expression of impassioned feeling must be kept imprisoned within the narrow confines of convention . . . . When I think of the attacks without number to which [the International Olympic Committee] has been subjected—the ambuscades, the unbelievable conspiracies, the mad jealousies. . . . I thrill to the realization that this sort of wrestling is great sport, even when our adversaries disregard the niceties of the classic techniques and go in for catch-as-catch-can methods. The important thing in life is not the victory, but the struggle; the essential thing is not to have conquered but to have fought well. To spread these precepts is to develop a more valiant, more strong, more scrupulous and more generous humanity.

The leading amateur athletic governing bodies from each country that had them were invited to send representatives to form the new Olympic organization. Many difficulties lay or were placed in the way of its success, but the doughty founder persisted and within three years the first Olympiad of the new series was held at Athens in 1896 with nine countries sending contestants. Under the new rules there was to be no age limit for competitors. The following events must be included in every Olympic competition: athletics (which by now had come to mean what we refer to in the United States as track and field and cross-country), gymnastics, boxing, fencing, shooting, wrestling, rowing, swimming, equestrian events, the modern pentathlon (running, riding, shooting, swimming, and fencing), cycling, weight-lifting, yachting, and competition in the fine arts (music, literature, art, sculpture, and architecture). Optional events have included soccer football, Rugby, polo, water polo, field hockey, handball, basketball, canoeing, and gliding. Other events such as tennis and archery have been included as demonstrations and then discontinued. In order to be eligible for inclusion in the Olympic program a sport must be practiced in at least 10 different countries, and at least 6 countries must indicate that they will enter contestants. Women appeared for the first time as competitors in swimming and diving events at Stockholm in 1912.

It is to be noted that the games are awarded by the Olympic Committee not to countries, but to individual cities. The second games were held in Paris. France, in 1900; the third in 1904 at St. Louis; 1906 at Athens, Greece, (a two-year interpolation not regarded as entirely official); 1908 at London, England; and 1912 at Stockholm, Sweden. War prevented holding of the games in 1916, but in a remarkable recovery Antwerp, Belgium, staged the games in 1920 to resume the series. Subsequent games were held at Paris in 1924; Amsterdam, Holland, in 1928; Los Angeles in 1932; and Berlin, Germany, in 1936. This time war interrupted the series for 12 years until London, in an unusual demonstration of courage and organizing ability, staged the games in 1948. Helsinki, Finland, carried on in 1952; this year the games go to Melbourne, Australia, and in 1960 will return to Europe to be held in Rome, Italy. A series of games to include only winter sports was inaugurated at Chamonix. France, in 1924 and has since been held at St. Moritz, Switzerland, in 1928; Lake Placid, N. Y., in 1932; Garmisch-Partenkirchen, Germany, in 1936; St. Moritz in 1948; Oslo, Norway, in 1952; and Cortina, Italy, in 1956. In 1960 the winter games will be held in Squaw Valley, Calif. Events that are currently part of the winter program are bobsledding (two-man and four-man), figure skating for men and women (individual and pairs), cross-country skiing (10 km. and 15 km. relay for women; 15, 30, 40, and 50 km. relay for men), downhill slalom and giant slalom skiing for men and women, ski jumping and Nordic combined (jumping and downhill skiing) for men only, speed skating (500, 1,500, 5,000 and 10,000 m. for men), and ice hockey.

At the early Greek games the winner was awarded a laurel wreath. Today he gets a gold medal. Silver and bronze medals are given for second and third places and certificates for fourth, fifth, and sixth places. Four hundred eighty-four competitors appeared at Athens in 1896 and most of them paid their own way. By the time of the games in Amsterdam in 1928, this number had increased to almost 4,000. Although only 1,700 contestants made the trip to Los Angeles in 1932, it was there that the construction of an Olympic village, especially built to house them, was introduced. This has now fortunately become a regular part of the program, since about 6,000 entered for the games in London in 1948 and more may be expected in Rome in 1960.

The fact that the games have maintained their amateur standing is best indicated by the disputes concerning professionalism that have arisen before and after each games. These disputes, although celebrated, are remarkable by being so few in number, indicating the strong hand that has been held by the Olympic Committee under the presidency of Baron de Coubertin and his successors. Americans will best remember the charges against the famous American Indian athlete, Jim Thorpe, who had startled the world by his remarkable performance in winning the decathlon at Stockholm in 1912. He had to return his medals and certificates, and his records were erased from the books. For some reason, long distance runners have been frequently involved in these disputes, and this year's case of Wes Santee serves to recall similar difficulties involving Paavo Nurmi of Finland and Jules Ladoumegue of France.

The current discussion as to whether the Russian teams should be considered professional, because they are subsidized by the state and because special considerations are given to athletes in training, has somehow missed the point, as Avery Brundage has pointed out. The International Olympic Committee has been preaching for 60 years the value of national programs of physical education and sports. The Russians are almost the only ones who have taken it seriously. Their athletes made such an outstanding showing in the Winter Olympic Games because as individuals they had trained hard and had entered their events in fine physical condition. The Olympic competition is an individual, not a national, matter.

Although there are team events in the various sports, there is no over-all team prize for the most events won or points scored by any particular country. The so-called unofficial point score for all events is strictly a product of newspaper manufacture, and the fact that the United States has more than once been adjudged the "victor" in this fashion is of absolutely no significance. All victories or outstanding performances are individual, no matter how much they may inflate national pride. No longer do we breach the walls of the city to receive home the Olympic victor as was once done in ancient Greece. Other honors are readily forthcoming, however, and the financial reward for the one who wishes to turn professional later may be, as in the case of some past skating champions, considerable.

U. S. Contributions

The United States has made some interesting and some outstanding contributions to the history of the modern games, among them the first winner to the modern series of Olympic games, who is still alive and active today at 87. He is James B. Connolly of Boston, who left Harvard and went with 11 other representatives from this country to win the hop, step, and jump championship at Athens in 1896. No other athlete has ever equaled the accomplishment of Ray C. Ewry of this country, who in four Olympic Games (1900, 1904, 1906, 1908) captured 10 gold medals in the standing high jump, broad jump, and hop, step, and jump events, which have since been discontinued. The outstanding individual performance recorded in the track and field events of one Olympic Games was turned in by Jesse Owens of the United States at Berlin in 1936, when he won gold medals in four events, the 100-m. and 200-m. dashes, 400-m. relay, and broad jump. His performance in each instance tied or broke or aided in breaking the Olympic record. These records have not since been exceeded in Olympic competition. No other athlete has ever exceeded his distance in the broad jump (26 ft. 5 5/16 in.) at any time except himself (26 ft. 8¼ in.). Bob Mathias is the only man ever to win the decathlon twice in the Olympic games (1948, 1952). In so doing he set a new record for points scored under the new system in his second try.

The current president of the International Olympic Committee is the first man from the United States elected to this important office. He is Avery Brundage, a formidable athlete in his own day, although never an Olympic victor, since he achieved his peak performances during World War I when no games were held. He won the United States all-around track championship in 1914, 1916, and 1918. This achievement is best measured by considering that this series of events required as much, if not more, skill and endurance than the Olympic decathlon and that they were all contested in one day rather than two days, as is the case in the decathlon.

Doctors and the Olympics

Physicians, both as graduates and as medical students, have won their share of victories at the Olympic Games. Probably the first to win the gold medal as a physician was G. E. Sheldon of the United States, who was springboard diving champion in 1904. An even more famous Olympic diving champion is Sammy Lee, an ophthalmologist in the U. S. Army Medical Corps, who won the high platform diving championship in 1948 and 1952. Also in the field of swimming, George Kojac of the United States, competing in the 1928 Olympics as a medical student, won the 100-m. backstroke, swam on the 800-m. relay team, and took fourth place in the 100-m. free style swim. In 1908 at London, J. R. Calkins of the United States was a member of the team that won the revolver and pistol-shooting titles at 50 and 100 yd. In 1932 at Los Angeles, John R. Huffman took sixth place in the saber event, an outstanding achievement in a sport so dominated by the Europeans. In 1952 Britton Chance of Philadelphia sailed his 5.5-m. yacht to victory at Helsinki.

Oddly enough, in track and field events, where one would least expect to see physicians or medical students as competitors because of the enormous amount of practice required, they have achieved some noteworthy performances. Paul Martin of Switzerland took second place in a thrilling 800-m. race at Paris in 1924 while he was a medical student. Patrick O'Callahan, now of Roseville, Ireland, won the Olympic hammer throw in 1928 and 1932. In 1936 John Lovelock of New Zealand, who was also holder of the world's outdoor records at one mile and 1,500 m., won the 1,500-m. race at Berlin. In 1948, Arthur Wint, a medical student from Jamaica, British West Indies, won the Olympic 400-m. crown.

As medical training and practice become more complex and demanding of time, we can expect to see fewer names of physicians as competitors and many less as victors in the Olympic Games. At the same time, the growing interest in the relationship between medical and physiological problems and athletic performances, which has led to the establishment of the International Federation for Sports Medicine, British Medical Sports Association, and the American College of Sports Medicine, assures us that there will be increasing participation of physicians as coaches, trainers, advisors and observers. Such distinguished sports buffs as Adolphe Abrams, medical advisor to Great Britain's Olympic teams for many years, may expect to be joined by many others who contribute their skill and knowledge as well as their enthusiasm to these international programs.

Even those physicians who have mental reserves about the medical value of sports, particularly athletics, may wish to ponder the effect in safeguarding mental health that might be produced if they could succeed in inculcating the qualities that at least one writer feels that they are capable of promoting:

> Loyalty that excludes taking refuge in subterfuges, docility and obedience to the wise commands of the director charged with the training of the team, the spirit of self-renunciation when one has to fade into the background in order that the interests of the team may thereby be furthered, fidelity to obligations undertaken, modesty in victory, sereness in adverse fortune, patience toward spectators who are not always moderate, justice if the competitive sport is bound up with financial interests resultant from voluntary agreements, and, in general, chastity and temperance already recomended by the ancients themselves.

These and other remarks were addressed to the Italian Sports Federation on the 10th anniversary of its revival last year by Pope Pius XII, who was an enthusiastic and skillful rider and swimmer as a young man and who was responsible for the installation of a gymnasium at the Vatican. Substance has already been lent to these words by the sportsman-like conduct of the many Olympic competitors from all over the world and their subsequent records as good citizens as well as good sportsmen. This year has already seen the great mile champion, John Landy of Australia, stop in the middle of an Olympic trial race to help a fallen competitor at the risk of losing his own place on the team. No one who was present at the opening of the Olympic Games in Helsinki in 1952 could ever forget the tremendous inspiration of that moment when the carefully guarded secret of the identity of the runner to bring the Olympic torch into the stadium was revealed. The incomparable Paavo Nurmi appeared in running clothes and circled the track before lighting the fire, while the huge crowd rose as one with a mighty roar of pride in this man who had so well exemplified their athletic ideal to the world in previous Olympic contests.

The interest and affection in which the Olympic games are held by such a great number of the world's people, and the strength that has enabled them to overcome the jealousies, bickering, and unfortunate occurrences that at first almost prevented their rebirth and later have at times marked their growth, is best epitomized in the Olympic Oath taken by all competitors at the start of the games. If all of our interest and activities in sports from the very beginning had produced nothing more than the desire to implement this oath, then it would have all been worthwhile. "We swear that we will take part in the Olympic Games in loyal competition, respecting the regulations which govern them and desirous of participating in them in the true spirit of sportsmanship for the honor of our country and for the glory of sport."

147 W. Main St.

THE INTERNATIONAL FEDERATION FOR SPORTS MEDICINE

Giuseppe La Cava, Rome, Italy

• *The Fédération Internationale Médico-Sportive (FIMS) first convened in 1928, when 33 physicians from 11 countries met in connection with the Winter Olympic Games. The organization has continued in spite of interruption by World War II. Its purpose has been to inaugurate relevant scientific research, to promote the study of medical problems encountered in sports and physical exercise, and to organize international congresses to be held simultaneously with the Olympic Games. The 11th International Congress was held this year in Luxembourg. The list of topics discussed in the past includes such problems as standard charts for examination and evaluation of athletes, tests of physical fitness, medical guidance in physical exercise, therapeutic exercise, orthopedics and traumatism, evaluation of physical education training, women in sports, and young people in competitive athletics. The FIMS has also been able to help with the organization of occasional scientific meetings and national conventions when help was needed by the organizing committees in various countries. In 1954 there were 23 national associations concerned with the diffusion of the concept of medicine related to sports.*

Physicians of different nations, guided by a common goal, that sports were to be a means of improving the health of mankind as a whole, met for discussion and soon formulated the idea of establishing a unique organization. Thus, the first medical congress dedicated to sports took place in March, 1915, in Paris. The topics it treated were the physiology of physical exercises and kinesitherapy. However, this good start was interrupted by World War I, which put an end to peaceful international relations. After World War I, when the Olympic Games were reestablished and the scope of their organization was enlarged, the sports physicians no longer limited their activity to the treatment of sick athletes and to emergency calls but began to engage in scientific reasearch and systematic tests on the finest champions of the world.

Organization and Purposes of Federation

On Feb. 14, 1928, at the time of the ninth Olympic Games, the first step in the founding of the Fédération Internationale Médico-Sportive (FIMS) was taken. On this occasion, in St. Moritz, Switzerland, where the Winter Olympic Games were being held, the first meeting of physicians took place; 33 physicians of 11 different nations participated. W. Knoll (Switzerland) was elected president; A. Mallwitz (Germany) secretary general; and F. J. J. Buytendijk (Holland), W. Dybowski (Poland), and Latarjet (France) members. Buytendijk was put in charge of the organization of the first International Congress on Sports Medicine, scheduled to take place in Amsterdam, the Netherlands, during the Summer Olympic Games in the month of August of the same year. The congress met with great success; 281 physicians and specialists in physical education, representing 20 different nations, were present. The first constitution of the Association Internationale Médico-Sportive (AIMS) was approved. Buytendijk was elected president. The constitution of the association contained the following purposes: (1) to inaugurate scientific research on biology, psychology, and sociology in their relation to sports; (2) to promote the study of medical problems encountered in physical exercises and in sports, to be done in collaboration with various sports federa-

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Director, National Institute for Sports Medicine, and Orthopedic Surgeon, Rivniti Hospital.

tions and organizations; and (3) to organize international congresses to be held simultaneously with the Olympic Games.

In October, 1930, the committee of the association, meeting at Vienna, Austria, chose Brown of New York to take charge of the second congress. The congress was scheduled for the time of the 10th Olympic Games, which were to be held in Los Angeles in 1932. This congress, however, did not take place, because the American physicians did not participate in the program planned by their European colleagues. The second convention, therefore, did not take place until September, 1933, when it was held at Turin, Italy. In the meantime Buytendijk had resigned, and Latarjet of Lyons, France, had been elected president. The topics to be discussed were divided according to subjects and grouped under nine headings, including anthropology and charts for evaluating physical fitness, organization of physical directors of different nations, kidneys and sports, respiration, fatigue, orthopedics and traumatism, and women and sports. It was on this occasion that an international association, with Latarjet as president, can be considered to have been duly established; the second article of the constitution was changed and the name of the association was changed to Fédération Internationale Médico-Sportive et Scientifique. It was also established that the general assembly was to meet every four years when the congresses were held. Congresses were to be organized at the time of the Olympic Games. Later this interval of four years was recognized as being too long.

For this reason French doctors interested in sports organized at Chamonix, France, in September, 1934, the third International Congress on Sports Medicine; eight different nations were represented. The following topics were discussed: issuance of a standard chart for medical evaluation of physical fitness, medical control of physical education and of sports, medical guidance in physical exercises, and sports engaged in at high altitudes.

At the same time the *International Bulletin* was established and new proposals were advanced, for instance, the teaching of physical education in all medical schools, with practical and theoretical lessons and final examinations; the awarding of a special diploma to those passing these examinations, enabling them to obtain positions such as those of hygienist and school doctor; the institution of a national and international licensing system for athletes with the approval of the associations for sports medicine of various countries (without such a license, the athletes were not to be allowed to participate in any international contest); and the standardization of medical diagnostic forms (minimal and maximal). Other changes were made in the constitution. The word scientific was eliminated from the name of the federation; article 11 of the constitution provided that the federation must meet at the same time and collaborate with the section on hygiene of the League of Nations.

The fourth International Congress on Sports Medicine was held during the 11th Olympic Games in 1936 in Berlin, Germany; 1,500 physicians of 40 nations met July 28 to 31. The topics, divided under nine headings and discussed in six different meetings, were metabolism and circulation; circulation and respiration; metabolism, training, and hygiene; psychology in sports; aviation medicine; medicine of physical education; traumatology and medical gymnastics, biometrics; and biological and social medicine.

The following year the French again organized an international congress, the fifth, which was held July 11-17, 1937. The topics discussed were divided into four categories: biology and sports, scholastic and postscholastic education, orientation in sports, and accidents in sports. At this congress, Latarjet and Knoll were elected honorary presidents, Conti (Germany) was elected president, Ugo Cassinis (Italy) secretary, and Albert Govaerts (Belgium) treasurer. The last convention prior to World War II was held in Brussels, Belgium, on July 9-12, 1939. The principal topic of discussion was biology applied to physical education and to sports; at this congress the number of the members of the committee was increased with the election of Paul A. Chailley-Bert (France), Hermann Brandt (Switzerland), Biezius (Lithuania), Plasch(Belgium), Dybowski (Poland), Emerich Szukovathy (Hungary), and Jiri Kral (Czechoslovakia). The organization of the seventh International Congress, which was supposed to take place in 1940 in Finland, was entrusted to Simo Antero Brofeldt of Helsinki. This congress never took place, because in the meantime World War II had begun.

Postwar Changes

After the war, Govaerts of Brussels, Belgium, the last vice-president of the federation, acting in accordance with the rules and regulations of the constitution approved in 1939, took the initiative and entrusted Kral of Prague, Czechoslovakia, with the duties of secretary general. The members of the committee, Chailley-Bert, Louis Merklen, Kral, B. A. McSwiney and Brandt, consented to a democratic reorganization of the federation. The new constitution was approved by the general assembly, which gathered in Brussels on June 21, 1947.

The seventh International Congress was held in Prague in 1948. At that time the wounds of the war were still open and bleeding. The spirits of all Europeans were still shaken; Europe itself was slowly recovering from the ruins of the war. Slowly the federation picked up, one after another, the threads of its web, which had been torn apart by the war. The congresses, which since that time have taken place successfully every two years, have become the foundation stones on which the magnificent edifice of modern sports medicine is developing. The eighth International Congress met in Montecatini, Florence, Italy, in 1950. It established the structural foundations of the new organization, giving it that democratic and universal spirit that has stimulated and determined the formation of many national associations for sports medicine. At this Congress the following topics were treated: physical education training and its evaluation, sports competition among young people, and reeducation of "traumatized" athletes. Govaerts was reelected president and I was elected secretary general. The ninth Congress took place at the Sorbonne in Paris, France, May 30-June 1, 1952; it demonstrated the high scientific level of the work and studies that had been carried on. The topics of the congress were surgical and nonsurgical treatment of traumatic lesions of the knee (fractures excluded) and the general syndrome of adaptation in sport activities.

The 10th International Congress in Belgrade, Yugoslavia, in 1954, in which a large number of legally represented national associations participated, gave proof of the solidarity so far attained by the federation. The topics treated were sport in mature age and sport and physical rehabilitation.

The 11th International Congress, which recently took place in Luxembourg on May 30-June 1, again confirmed the fundamentally scientific and moral aspect of the branch of medicine that deals with sports. Sports medicine, as a discipline, has gained autonomy among the medical and biological sciences. At this last congress, the following topics were discussed: lesions of the muscles and of the tendons and standardization of the cardiofunctional tests in sports.

At present the executive committee of the federation is composed of Chailley-Bert (Paris), honorary president; A Govaerts (Belgium), president; G. La Cava (Rome), executive secretary; Kral (Prague) vice-president; Tegner (London), vice-president; Jones (Luxembourg), treasurer; and Kriatchko (U.S.S.R.), Koch (Germany), Prokop (Austria), and Smodlaka (Yugoslavia), members.

Recent Activities

In recent years the activities of the federation have followed two essential directions. The first is concerned with the progress of the studies made by that branch of medicine that is related to sports. The federation has sponsored scientific meetings and national conventions; it has encouraged worthwhile undertakings and has given help for their successful realization whenever this was needed by the organizing committees. We must remember, among other meetings of international character, the successful Argentine Congress for Sports Medicine, which took place in Buenos Aires; the symposium held in Berne, Switzerland, on the occasion of the European athletic contests; the congresses of the German Association for Sports Medicine held at Edenkoben, Augsburg, and Freudenstadt; the scientific meetings of the British Association for Sports Medicine; the courses on sports medicine held in different nations, as in Austria, Yugoslavia, and Switzerland; the national Italian congresses of Trieste and Perugia; the international meetings of Turin, Italy, on the occasion of the European swimming championship; of Cortina, Italy, on the occasion of the seventh Winter Olympic Games; and of Sestriere, Italy, dedicated to winter sports; the meetings of the Commission on Sports Pedagogy of the European Center for Culture in Geneva, Switzerland; and the convention on sports medicine organized by the Ministry of Physical Education and Sports of Luxembourg.

The initiative of the Italian Federation for Sports Medicine is also to be pointed out. This federation publishes every two years an international bibliography that brings together everything in the field of sports medicine that is published in the world. The same can be said also for the journal *Medicinea Sportiva,* which each month publishes the international federation's *International Bulletin.* This journal. together with many other specialized publications dealing with medicine relating to sports—French, German, Belgian, Yugoslavian, and Argentine—keeps alive in the members of the federation the spark that kindles the fire of scientific and clinical research and works for the solution of the important moral, social. and educational problems connected with the development of sports in the modern world.

The second is concerned with the diffusion of the concept of medicine related to sports and with the propaganda for the establishment of national associations in different countries. The results have been very good. While in 1950 in Montecatini there were only 6 such regular associations, in 1952 the number went up to 13 and in 1954 to 23, and with the recent admission of Australia, Bulgaria, Chile, and Rumania and the eventual admission of Canada, Poland, and Hungary, the number of national associations will go up to 30. This undoubtedly makes for success, yet it is not to be considered as a point of arrival but rather as a stage in the establishment of national associations in all countries where sports and physical education are practiced.

The task of spreading the concept of sports medicine was greatly helped by the official recognition of the federation received in Oslo, Norway, in 1952 from the International Committee on Olympic Games. The high prestige of the committee was especially stimulating and helpful to the efforts of the federation in establishing relations among international sports federations. A very detailed program along these lines was recently proposed by the general assembly of the federation on the occasion of the 11th International Congress in Luxembourg; its fundamental points are (1) participation of a medical representation or a medical commission in each international sports federation and (2) the establishment of a technical committee in the FIMS composed of the abovementioned medical representatives for the coordination of the sports and medical activities. A direct liaison between sports federations and the international federation would thus be feasible through the most qualified representatives. The federation could accomplish its duty as a unique specific consultative body in the field of sports medicine recognized by the International Olympic Committee. This general program has been outlined by the president of the committee, Avery Brundage, whom we thank for the interest and good will with which he follows our work. The good results that have already been obtained by some federations like the International Association of Amateur Boxing and the efforts made by other associations (of athletics in general and of swimming) hold out hope for the definitive completion of this program and for the realization of those objective ideals that modern sports medicine has encouraged by its spontaneous, vital initiative.

Viale Pinturicchio 58.

J.A.M.A., November 17, 1956

A MEDICAL HISTORY OF GYMNASTICS

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• The medical profession has always been interested in exercise, not only for recreation and as an aid to physical development but also as a prevention against disease. This article introduces a modified symposium on athletics both as sport and for the furtherment of health.

The history of physical exercise, especially when reviewed in a medical vein, reveals the logic behind gymnastics as part of the curriculum to strengthen the entire body. Much of physical exercise as we know it today has been, and still is, formulated by the physician, on the basis of sound medical principles.

The history of man's interest in voluntary coordinated exercise of all sorts from the most ancient recorded history to modern times is embodied in the study of the origin and development of gymnastics. This word of Greek origin derives from the circumstance that the competitors exercised naked. Hence, their place of exercise became the gymnasium, a public building, as opposed to the palaestra, a private school where boys were trained in physical exercise. An athlete in ancient Greece was originally one who contended for a prize in the Olympic Games, whether in musical, gymnastic, equestrian, or other competition. Later, only those who competed in the gymnastic contests were designated athletes. The story of the development of gymnastics is also the story of the interest of doctors of medicine in exercises designed not only for recreation but also to aid in physical development as a preventive of, or countermeasure to, disease.

This story has been summarized succinctly in a series of articles written by Ludwig H. Joseph, M.D., and published under the title "A Medical History of Gymnastics" in *Ciba Symposia*, March-April, 1949. With the permission of the editors of that magazine, these articles have been condensed into one and are presented here with a group of essays that signalize the continued interest of the medical profession in sport and athletics of all kinds.

Gymnastics from the Middle Ages to the 18th Century

Since its origin in antiquity, the concept of gymnastics has not been uniform. Educational and medical gymnastics were already known to the Greeks. Generally speaking, all definitions of gymnastics can be reduced to two: first, that every intensified movement is gymnastic exercise (Oribasius of Pergamon, 326-403 A.D.); and, second, that in each exercise there is the idea of active volition (Galen and Avicenna). The concept of medical gymnastics included all healthful and health-furthering exercises. For this reason physicians at all times advised the avoidance of any exaggerated activity, particularly professional athletics. The concept includes both preventive and therapeutic gymnastics, the latter including gymnastics for the sick, weak, and elderly. Herodicus (fifth century B.C.) was reproached by Hippocrates for treating patients with fever by gymnastics. Asclepiades (128-68 B.C.) used gymnastics in connection with massage and dietetics.

The Early Middle Ages.—During the Middle Ages, the gymnastic practices of the classic Greco-Roman era were forgotten, but the idea of curative gymnastics was not entirely lost in medical circles. The first medieval health book, "Regimen Sanitatis Salernitanum," twice mentioned exercises as therapeutic measures. The governing feudal class was obliged to care for the physical education of its members who, for the most part, were soldiers. A boy's physical education began at 14 with vigorous sports and exercises, including dancing, and the most important premilitary exercise was horsemanship. The exercises of the medieval nobleman were the seven mentioned in the "Mirror of Knights": (1) riding with rapid mounting and dismounting; (2) swimming and diving; (3) shooting with the bow and crossbow; (4) climbing on ropes, poles, and ladders; (5) fencing, wrestling, pushing stones, and jumping; (6) dancing; and (7) tournaments. The ordinary citizens and craftsmen also applied themselves to the first six varieties. Acrobatics by professional performers were a principal form of entertainment.

The Renaissance.—Classic gymnastics revived with the Renaissance and the rediscovery of Greek and Roman literature. With their increasing study, educational theory tried to achieve the aim of classical education: the man of vigor and wisdom. For this reason, the great teachers of humanism consciously introduced gymnastics into their educational program. Petrarch (1304-1374) in his pamphlet, "Against a Certain Physician," expressed the idea of substituting a natural therapy, such as exercise, for medical remedies that poison the body. Vittorino Da Feltre (1378-1446) made gymnastics obligatory in his educational program. In addition to his knowledge of medicine, he was learned in philosophy, science, mathematics, Latin, and Greek. Under the patronage of the Duke of Mantua he founded an educational institute in the country for children of the nobility and the poorer classes as well, where physical education preceded intellectual training. He selected for each student a type of exercise especially suited for his body, his age, the season, and the time of day. He was especially proud of the fact that he succeeded in changing the bodily constitution completely by means of special exercises in connection with dietetics. In general the exercises employed were riding, fencing, swimming, dancing, wrestling, running, jumping, archery, throwing the discus, ball games, hunting, fishing, and mock battles between two parties. All the games were played outdoors in both summer and winter. Vittorino left no writings, but his doctrine changed the spirit of all later education completely. This doctrine had the purpose of bringing to the highest perfection the three essential elements of man: body, mind, and soul. The introduction of gymnastics into the educational program was considered an indispensable preliminary condition for educational success.

Cardinal Aeneas Sylvius Piccolomini, later Pope Pius II (1404-1464), inveighed against the decay of the physical education that ought to precede spiritual education. For hardening purposes he recommended life in the country from time to time, physical work in the open air, and plain food. He considered hunting a sport especially suitable for physical education, since it is connected with a considerable number of exercises, such as riding, climbing, swimming, shooting with the bow, and hurling the spear, as well as hardening against the effects of weather. Francesco Barbaro (1395-1440) considered not only the spiritual but also the physical condition of both parents as highly important for the health of their child and therefore recommended physical exercise for young women too. Parents were also interested in play for their children so as to attain a healthy development of the body. Leon Battista Alberti (1404-1472) called special attention to physical exercise as of the highest importance even in early infancy. He recognized that thus the muscles are strengthened, the nerves become accustomed to strain, the blood circulates more quickly; in short, the whole physical being becomes more lively. In the daily plan of studies of Duke Philibert of Savoy prepared by Philelphus, a peripatetic teacher, two hours for gymnastics and games were allowed, including running, softball, and football. Florentine football was played in the principal square of the city in a sort of stockade by two bands of youths selected from honored soldiers, gentlemen, seigneurs, and princes. According to Bardi, "a good player should play his game with easy and sprightly grace, in the which he will easily succeed if he proceeds in all his actions with moderation and without passion."

Maffeus Vegius (1407-1458) in his book, "Education of Children and Their Good Habits," distinguished strictly two sorts of exercises: those that serve as recreation from intellectual work, and those whose purpose is the strengthening of the body. The former should be of a lighter nature; the others, including military exercises, require greater efforts. He wished to avoid heavy athletics, suggested moderation in all actions, and rejected exaggerated exercises. Juan Luis Vives (1492-1540) in the fourth book of his work, "On Instruction and on Christian Education," stressed exercise as indispensable for young students. He proposed long, rapid walks, running, jumping, and throwing the discus. He emphasized expressly that all exercises must be executed not in a military but rather in an educational manner; that they are not to be carried on to such a degree as to produce intellectual fatigue; and that, on the contrary, they should refresh the young men and stimulate them to new intellectual power.

Medical Gymnastics in the 16th and 17th Centuries

The humanistic educators had linked gymnastics so closely with education in general that it was no longer possible to eliminate it from the educational program. But their doctrines did not fructify the medical discipline, because medicine was still highly dogmatic and scholastic during this period. Physicians in the 15th century were skeptical about the use of gymnastics. Generally, it is characteristic of the position of medicine during the Renaissance that it did little to advance gymnastics, recommending only the lightest exercise. The great changes in culture and mode of life at the end of the 15th century and the beginning of the 16th century marked the end of the Middle Ages. Although the original Greek documents on medical subjects were brought to light in the 15th century, the results of their study appeared only gradually. On the other hand, such inventions as gunpowder and the art of printing produced an effect on the people of that period as revolutionary as the discovery of atomic energy today. The art of printing made possible criticism and interpretation of the classical writings in a new sense and facilitated the propagation of such knowledge in larger scientific circles than ever before. Moreover, a general fever of inquiry seized many physicians.

Influence of Mercurialis.—Hieronymus Mercurialis (1530-1606), with his "Six Books on the Art of Gymnastics," stood as sponsor to medical gymnastics. Characteristic of this work is the fact that every exercise is considered from the viewpoint of its usefulness to health, since he considered all gymnastics of only medical value. For him, the only exercises of interest to physicians are those characterized by introduction of the conscious will, and particularly by strenuous breathing and vehement movement. Mercurialis classified gymnastics into two kinds, corresponding to kinds of medicine, preventive (or conservative) and therapeutic gymnastics. Conservative gymnastics is for the healthy, therapeutic gymnastics for the sick. In the first place, the quality and the quantity of exercise should be accommodated to each constitution. Preventive and curative gymnastics both make use of a purely physiological remedy, movement. On the contrary, drugs, especially the medieval medicaments, poisoned and weakened the body. Based upon the Hippocratic definition of health as harmony of the humours, the aim of every healthy exercise is to maintain this harmony. Strenuous military exercises are therefore not always suitable, even for healthy bodies. Athletics is indirectly injurious to health. These injuries arise from defective nutrition associated with training, namely, excessive meat-eating; from suppression of normal sexual life; and from the effect on the lungs of dust inhaled in the arena.

Mercurialis set up the following principles for medical gymnastics: 1. Each exercise should preserve the existent normal healthy state. 2. Exercise should not disturb the harmony between the principal humours. 3. Each exercise should be suited to certain fixed parts of the body. 4. All healthy people must be interested in gymnastics and regular exercise. 5. Sick people are permitted only such exercises as do not exacerbate the existing condition of the patient; exact diagnosis must be the basis for such individualized treatment. 6. Convalescents and weak and older persons should have special exercises. 7. Persons who lead a sedentary life, as well as scientists and prisoners, urgently need gymnastics. For medical gymnastics he thought that spring and autumn are particularly suitable, and the winter even more, for vigorous exercises. In the summer months the early morning, in the winter the later hours of the morning are to be preferred for exercise. Such activity should always be carried on in the open air in a place sheltered from the wind. It is good to clean the body thoroughly, even to take a purge before exercise, but exercise on an empty stomach is to be avoided. Gymnastics should strengthen not only the muscles but also the nerves, and should further sleep. According to Mercurialis, ball games strengthen the arms, the back, and the intercostal muscles and, therefore, are fit for convalescents, weak persons, and even for wet-nurses and epileptics. He discusses other kinds of exercise. Thus he distinguishes three sorts of walking: walking to and fro, in the sense of the Greek peripatetics, in order to stimulate intellectual conversation; then, more intensive walking, to aid digestion or to work up an appetite; finally, mountain climbing, because it is diaphoretic, to alleviate paralysis of the legs.

Merculialis considered running a very healthy exercise, when performed without carrying a burden and not over hurdles, and he thought running at night particularly healthy, because the body does not suffer the heat of the sun. This exercise strengthens the muscles and also the digestion. He recommended throwing the discus for the wrists of arthritic patients, especially, and for strengthening of the muscles of the legs, arms, hips, and back. Jumping he considered suitable for both sexes, though contraindicated for patients with pulmonary disease and pregnant women. Jumping with dumb-bells to increase the swing he considered unhealthy. Accompanied by music, gymnastics has a calming effect on the nerves. Athletic exercises, including hand springs, are to be rejected, as these push the intestines against the diaphragm. Only rope climbing and wrestling are wholesome. Very interesting, from the medical viewpoint, is the recommendation of passive gymnastics for patients confined to bed for a long time. This was to be achieved through the use of swinging beds, like hammocks. Like some modern physicians, he included in his work exercises of the voice, respiration, and even the eyes. Passive movements of the body on board ship, connected with the psychological effect of changing surroundings, Mercurialis considered wholesome for diseases of the lungs, larynx, and skin, as well as for headaches.

Followers of Mercurialis.—All books on gymnastics of the next centuries are based on this standard work of Mercurialis. The most original work after him in the field of gymnastics is devoted specifically to a single exercise, jumping. Entitled "Three Dialogues on the Acrobatics of Jumping by Saint Archange Tuccaro" (born about 1535), it mentions 53 varieties of jumping. Tuccaro tried to make the body flexible in youth. Although not a physician, he pointed out the medical benefit to be derived from this exercise. "This robust and strong exercise has a tendency to expel excrements and to calm all sorts of humours." Ambroise Paré (1510-1590), the famous surgeon, dealt in detail with movement and repose in the introduction to his "Surgery." He referred to the doctrine of Galen that the body needs exercise for health. In accordance with the theory of the humours, he reserved heavy exercise for large, cold-humoured persons, lighter exercise for thin and temperate ones. As did Mercurialis, he included breathing exercises and massage in gymnastics. Moderate exercise was to be taken before meals to help the digestion. Oddly enough, Paré added carrying of burdens to the usual exercises, such as running and riding. Not only did he consider gymnastics a part of general hygiene but, as a surgeon, he felt that exercise of the limbs, especially after fractures, was indispensable. He suggested light exercises for diseases of the kidney and bladder and for gout.

Joseph Duchesne (born 1544), who was physician to the court of Henry IV of France, wrote on exercise in his "Ars Medica Hermetica": "The essential purpose of gymnastics for the body is its deliverance from superfluous humours, the regulation of digestion, the strengthening of the heart and the joints, the opening of the pores of the skin, and the stronger circulation of blood in the lungs by strenuous breathing." Here, for the first time, we find swimming included on an equal basis with other exercises. It is contraindicated in cases of melancholy and diseases of the lungs but is considered as generally strengthening the body. Walking is recommended, particularly for those older persons who were formerly accustomed to more strenuous exercises. In his "Gymnastic Exercises," Laurent Joubert (1529-1583) attached great importance to daily exercises. As professor of medicine of the University of Montpellier, he was occupied particularly with the problem of introducing gymnastics and its use into the medical course. He considered physicians the only ones capable of prescribing gymnastics, rather than teachers and educators, whom he regarded as insufficiently educated. In the second book of Marsilius Cagnatus' "Preservation of Health," published at Padua in 1605, rowing is introduced into medical gymnastics for the first time.

Physiology and Gymnastics.—Physiology gave gymnastics a scientific basis, liberating it from empiricism. Sanctorius Sanctorius (1561-1636), physician of Padua, was first to study scientifically the body during perspiration. Attendant upon the progress of mechanics, there developed an increasing interest in human and animal movement. The literature on this subject began with Jean Canappe's short essay, "The Movements of the Muscles," published in 1546. The great progress in the physiology of the muscles continued into the 17th century. Many medical works covered this subject, for instance, Claude Perrault's "Mechanics of Animals" (1680), Ulisse Aldrovandi's "On Quadrupeds," Fabricius ab Acquapendente's "Movement of Animals" (1614), and the book on animal movements by Antoine Deusing (1612-1666). Girolamo Cardano's (1501-1576) theory of the movement of the muscles is conceived entirely from a mathematical-mechanical standpoint. He himself practiced gymnastics daily. He recommended light exercise for pregnant women, swimming, but no exercise for older men.

Gymnastics in the Pre-Revolutionary 18th Century

The 18th century is characterized by the Enlightenment and the movement for a return to Nature. Representative of the Enlightenment is the great "Encyclopedia" of Diderot and D'Alembert. Volume 7 of the 1757 edition contains the following definition of gymnastics: "men acquire bodily force and agility by different means for different purposes." Military gymnastics arose from the need of men to assure their safety. Medical gymnastics arose from the need of men to take care of their health with suitable exercises ordered by physicians. Athletic gymnastics grew out of the desire to give public exhibitions of strength and agility. Regarding gymnastic medicine the dictionary adds: "medical gymnastics, although simple in origin, became too complicated in practice, and ended in an excess of luxury, effeminacy, and voluptuousness." The life of the upper classes was never as artificial as in this rococo period. It is especially remarkable, therefore, that, despite all such customs, even in these times, gymnastics did not disappear entirely from the educational program.

Nicolas Andry (1658-1747), professor of medicine at the Royal College of Paris, in his "Orthopédie" took an entirely new road. The word orthopedics was introduced to medicine by this author. The subtitle makes clear to us the purpose of the author: "the art of preventing and correcting the deformities of children's bodies." Andry advises parents to pay attention to the bodily development, even of infants. He recommends special exercises to obtain large flat collarbones and a well-shaped chest. These consist in stretching the arms with wands, lifting up a rope reaching to the ground, and holding the wand extended horizontally. The spine is to be made flexible by flexion over the lap or the knees. This exercise with the hands on the ground, made without any assistance, is known in gymnastic nomenclature as the bridge. In general, to prevent deformities or to cure present ones, Andry recommended exercise of the legs or the arms, with or without wands, carried out very energetically in case of paralysis or after fractures. While he recommended for the children of the upper classes such exercises as riding and hunting, for the poorer classes he proposed rural work as a substitute for gymnastics.

Sabbathier in 1772 deplored the bad habits of his time, urged moderate gymnastics for convalescent and weak persons, but rejected all athletic exercises as unhealthy. In England, Francis Fuller, in his "Gymnastic Medicine" of 1705, lamented the decay of physical education and medical gymnastics. In Germany, the physician Johan Zacharias Platner in his "Gymnastics of Antiquity" (1724) bitterly expressed the opinion that his time hardly appreciated healthy daily exercises and that all sense of the necessity of gymnastics to preserve a healthy body was lost. Joseph Tissot (1756-1826), a French military surgeon, called his work "Medical and Surgical Gymnastics" and described it as an essay on the usefulness of movement, on different exercises, and on repose in the cure of diseases. He said that moderate gymnastics gradually produced a lasting result but that, on the other hand, strongly exaggerated exercise was injurious to muscles and internal organs, through excessive wear and tear. Therapeutic gymnastics is indicated especially for rheumatism and gout. During convalescence from chronic diseases, he suggested slow and gradually increasing bed exercises. He proposed exercise even during convalescence from abdominal diseases. Gymnastics was to be supplemented by massage, especially before swimming, and by relaxation afterwards.

Giuseppe Nenci, professor of medicine at the University of Siena, in his "Discussion on Gymnastics with Regard to Its Use in Medical Practice" (1766) advocated curative gymnastics, which, in contrast to drugs and surgical therapy, is less energetic, particularly if used gradually and individually. Life and health consist in a continuous but equilibrated movement of fluids distributed into innumerable channels of the body. During this continuous movement, some parts are dispersed or must disappear entirely. Therefore, they must be supplied by others through alimentation. It is perspiration, on one hand, and a correct distribution of fluids, on the other, which leads the necessary introduction of new humours. Moreover, the alternating extension and contraction of the muscles extracts the blood from the veins of the heart and the lungs; in this way they facilitate the entrance of fresh blood into arteries. Therefore, gymnastics is the necessary precondition for the provision of blood to the whole body. Practically, this fact is manifested by an augmented diaphoresis and opening of the pores of the skin. This has a therapeutic effect on skin diseases, obesity, gout, and dropsy, which are characteristic diseases of blood stagnation. Nenci suggested light daily exercises for intellectual workers, older persons, and delicate women. Long walks or riding, which he considered the most natural exercises, are beneficial to both body and mind.

Summary

Looking at the development of gymnastics from the early Middle Ages on to the beginning of our modern era, one can see that, after the decay of antiquity, physical education had to be built up anew. The influence of classic gymnastics emerged only in the Renaissance. Seldom in the history of human culture has the intellectual climate been changed so consciously as in the epoch of Humanism and the Renaissance. The education of the Western European youth was based consciously on the Greek ideal of man, found anew in works of art, literature, and science. It was a natural consequence, therefore, that educational gymnastics appeared. Its aim—to harmonize intellectual and physical education, in which is included also the psychic influence of exercise—henceforth remains the basis of every successful educational program.

The medical use of gymnastics could be understood only in a period when medicine began to emancipate itself from the fetters of dogmatism. Just as the time was ripe for a Columbus to discover America, so it became mature for a Mercurialis to establish medical gymnastics, and to consider exercise only from a medical and hygienic standpoint. This medical appreciation was at first empirical. But at the end of the 17th century, stimulated by the progress of physiology, attempts were made to give to exercise a scientific basis. The 18th century provided social influences that showed new purposes for gymnastics. Orthopedic gymnastics arose from the unnatural clothing of this period and the deformities of the body connected with it. Orthopedic gymnastics leads directly to the Swedish gymnastics of our time. Thus medical gymnastics reached its definitive form in the period before the French Revolution.

147 W. Main St.

J.A.M.A., November 17, 1956

PHYSICAL FITNESS FOR ALL

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• *There is evidence of continued neglect of those activities whereby men and women should strive to maintain a healthful degree of physical strength, agility, and endurance. A lack of physical fitness limits one's opportunities for a full enjoyment of professional and personal life. Formal exercises can take the place, to some extent, of physical work. A planned program of exercises can be adapted to the individual's age, and, by progressing from a cautious beginning, it can be developed sufficiently to undo the mischief of long periods of neglect. The physical activity also results in certain mental satisfactions that make for a feeling of alertness and power. A set of exercises chosen from those herein described can increase the individual's ability to meet the day's physical and mental tasks.*

What is meant by physical fitness? Certainly, during the past year, that term has been uppermost in the minds of all Americans for many reasons. Coronary disease is prevalent in both men and women; statistics revealed by the Kraus-Weber experiments indicate the lack of fitness in the American boy and girl; the school programs of physical education fail to concentrate upon the physical development of all students and emphasize instead the few who are well-skilled in athletics; and the American people continue to prefer being spectators instead of participants in sports. All this points to the necessity of reeducating the public to the importance of a well-conditioned body. To be physically fit an individual must have a good capacity for performance and endurance, sound physique and smoothly functioning organs, and adequate muscular strength; strength, speed, agility, and endurance must be a part of each individual. Each day holds a responsibility to go forward toward maximum fitness whether the future holds war or peace, a soft life or a hard life. The individual can fit only into such a niche as demands the capacity he possesses, so that the greater his fitness and his ability to maintain it at his peak capacity, the more life's doors will open to him. Fitness to enjoy life to its fullest—physically, emotionally, and spiritually—is the fitness that each individual really wants.

Too many American people have neglected to engage in regular systematic exercise. Few men (except when there is a war at hand) make an effort to reach and maintain top physical condition. Only the 10 or 15% of boys and young men in the secondary schools and colleges who are out for varsity teams get in fairly good condition. The other 85 or 90%, as a rule, do not attain a high degree of physical fitness. The percentage of Americans who lack this high degree of physical fitness becomes much higher when we limit our study to men and women over 30 years of age. Although America is known as the land of sports, there is not a widespread intensive participation in sports on the part of the majority. A visit to any of our large bathing beaches during the summer will reveal thousands of individuals clad in bathing suits and lying on the sand, but few of them actually swimming. Probably many of them do not know how to swim, and, of those who do, a swim of 10 or 15 yd. at a time is the usual limit. Then, too, there are many sports spectacles in this country, but, except for the few players who are participating, there is not much exercise taking place. So it is obvious that too many people function below their normal capacity. It seems essential that, if we desire to get the most out of life, we must learn to increase the demands on the body and develop greater power, strength, and endurance for sustained effort. We must work for poise and skill in the use of our bodies.

Benefits of Exercise

There is no doubt that exercise benefits the body in many ways. Physical strength and general body conditioning are essential for growing boys and girls. Sufficient strength, particularly in the arms and shoulder girdle, the abdomen, and the pelvic girdle—a basic torso strength of all large muscle mass—is essential in order to have good control of the body. Participation in various sports, either for conditioning exercises or for body building, must be considered as one means of attaining such strength. Formal exercise can accomplish the same goal. It is a well-known fact that an individual is much more efficient in the performance of a skill if the muscles involved are in the best of condition. This implies specific concentration upon their development. The physical benefits of such exercises are improved posture, flexibility, agility, good balance, increased strength, and endurance. The functions of the various systems of the body are improved by exercise. For example, the general circulation of the body is accelerated, and the improvement results in food and oxygen being carried more efficiently to the body tissues.

In addition to physical development, exercise has a soothing effect upon the nervous system. During exercise the nervous system becomes more active than during sedentary mental work, but less fatigue results because the physical fatigue that comes from vigorous exercise serves as a mental tonic. Furthermore, a person who is physically fit does not have to apologize for being unable to engage in an activity, and he often finds himself able to do many things formerly considered beyond his capacity. Finally, when the desire for activity has been satisfied through the performance of wholesome physical activities, significant mental satisfactions follow. The person who is physically fit has an indescribable feeling of virility and power. He is much better prepared for meeting the problems of his day than if he were "soft" and out of condition.

Exercise also is an organic means of remedying the past neglect of the body, for, even if the body has not been given sufficient exercise, nature quickly helps to repair this past neglect. A program of exercise that involves the large muscles of the body and is not too severe at the start soon causes the body to respond. The organic systems begin to show new energy, the muscular system begins to become better toned, and

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the flesh becomes more firm. Gradually the body shows greater endurance and more capacity for work, and there is a rapid recovery from fatigue.

Planning an Exercise Program

The primitive man had little choice in the matter of exercise; if he wished to survive he had to engage in many forms of activity. Today it is different. One must plan to allow time for healthful exercise, and this exercise must be adapted to one's age and present physical condition. When one has done little or no systematic exercising, he must naturally go easy at first, for perhaps three or four weeks. Especially after an individual reaches 25 or 30 years of age, exercising must be gradual, because the muscles and arteries lose some of their elasticity and are unable to withstand the strain of sudden or prolonged vigorous activity. Regularity of exercise, however, is the important factor, along with this gradual increase in difficulty.

Adapting the type and amount of exercise to the individual must be stressed. The busy person who can give only a little time each day to physical exercise might do well to select an exercise for each part of the body: for posture; for strengthening the abdomen; for arms, shoulders, and legs; and for raising the chest and strengthening the muscles of the upper back. Such a routine might include exercises from a supine position, such as pelvic rolls, sit-ups, raising the knees, rotating the knees, or the exercise in which the toe touches the opposite extended arm. From a prone position, such exercises as hip raising (jackknifing the body up and down) or chin-up (lifting the head) would be helpful. Also, the individual might try the following exercises: sitting with legs straight, he might stretch by bending his trunk forward; sitting with his hands behind his head, twist his trunk; or squatting, imitate a jumping jack.

The general rule, "remember your age," must be adopted, because men and women under 30 may exercise with more speed and endurance than those over 30. After 30, one should work for endurance and not for speed. Just as "an apple a day keeps the doctor away," so a little regular and systematic exercise each day will help the individual to meet daily tasks with a better body and a more alert mind.

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EFFECT OF WARMING-UP UPON PHYSICAL PERFORMANCE

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• *Three methods of warming-up were compared as to their effects on the time required for seven athletes in a 440-yd. (402-m.) run. The means were obtained from 20 runs after five minutes of deep massage of each leg, 20 runs after five minutes of superficial massage (digital stroking) of each leg, and 20 runs after preliminary exercise. The differences found among these three methods of warming-up were statistically not significant. In a second experiment the performance of five runners in the 440-yd. run without warming-up exercise was compared with their performance after superficial massage; again the difference was insignificant. In a third experiment, an attempt was made to verify reports of other investigators that warming up by preliminary exercise improved performance; the test consisted of completing 35 pedal revolutions of a bicycle ergometer in the shortest possible time, the amount of work being 956 kg.-m. The warming-up exercise consisted of 60 pedal revolutions per minute for five minutes with a load of 5.5 lb. (2.5 kg.); it increased the mean muscle temperature by 1.3 C (2.3 F), but the effect upon performance again was not significant. Outstanding performances in the first experiment were made by men who had warmed up by deep massage, but an outstanding performance in the second experiment was made by a man who had not done any preliminary warming-up. In these experiments neither deep or superficial massage nor preliminary exercise improved the time of running; there was no evidence that massage had a beneficial psychological effect on the runner or that preliminary exercise improved sprint performance on the bicycle ergometer.*

It is almost axiomatic with coaches and athletes that a preliminary warming-up is indispensable for a good performance. The type and duration of warming-up varies, depending upon the country, the coach, the sport, and the individual preference of the athlete. Warming-up may be subdivided into two types, general and formal. In the general type, one may use exercises involving large groups of muscles, massages, hot showers, or other devices to raise the temperature of the body. In the formal type, warming-up consists of the movements that are used in the actual performance.

Two reasons are advanced for general warming-up. It is said that the strength and speed of muscular contraction increase with a rise in muscle temperature, and that the possibility of injury due to sudden forceful muscular contraction is lessened. The formal warming-up is credited with an improvement of coordination. While there seems to be general agreement regarding the importance of the formal type of warming-up, the effects of general warming-up may be questioned. True, no one will question the beneficial effect of warming-up when limbs may be almost numb from cold, but there is a suspicion that the practice of warming-up is frequently overdone.

To our knowledge no objective evidence has been presented that warming-up reduces the number of athletic injuries. As to the experimental evidence of an improvement in performance resulting from warming-up, there have been few studies reported. Asmussen and Bøje[1] studied the effect of preliminary work,

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Read in part before the annual meeting of the American College of Sports Medicine, Chicago, March 24, 1956.

short-wave diathermy, hot shower, bath, and massage upon performance on the bicycle ergometer. All methods of warming-up, except massage, were reported to be beneficial in both sprint and endurance rides. Schmid,[2] on the other hand, reported that not only setting-up exercises, hot bath, diathermy, and shower with alternating hot and cold water but also massage improved performance of both men and women in swimming 50 m., running 100 m., and riding the bicycle ergometer. Simonson and co-workers [3] also found that preliminary exercise improved running time of the 100-m. run for both men and women.

Malarecki [4] reported that not only actual warming-up exercises but merely imaginary exercises increased the speed of running 60 m. Hipple,[5] on the other hand, found that preliminary running had no beneficial effect upon the speed of a 50-yd. run. Carlile [6] reported that an eight-minute hot shower caused a 1% improvement in swimming 40 yd. The scholarly report of Asmussen and Bøje was most convincing. However, their negative findings regarding the effect of massage prompted us to investigate the effect of this type of warming-up. This investigation lead to two additional ones. Thus this paper represents a report on three series of experiments.

First Experiment

On the evidence presented by the previous investigators it was assumed that, except for massage, the various methods of warming-up beneficially affected physical performance. Therefore, the first study was designed to compare the effect of deep massage with that of preliminary exercise upon time of running 440 yd. In order to detect any possible psychological effect of massage, we decided to use performance after a light superficial digital stroking as a control.

Procedure.—Seven track athletes of Springfield College were used as subjects. All had previously run the required distance of 440 yd., and all were members of the freshman or varsity track teams. Each subject warmed up and performed individually on an outdoor track. A total of 60 test runs was made, 20 after deep massage, 20 after preliminary exercises, and 20 after digital stroking.

Digital stroking consisted of slow, gentle, rhythmic, and centripetal stroking covering the entire leg for a five-minute period. When deep massage was used, a five-minute general massage of each leg was administered. The same investigator served as masseur in all cases. Preliminary exercises included jogging 440 yd., setting-up exercises, and short sprints of 20, 30, and 50 yd. This warming-up took approximately 10 minutes. In deciding on the duration of warming-up, we were influenced by the findings of Asmussen and Bøje, who reported that the first five-minute period had the greatest effect. To be safe, we doubled this period.

Three afternoons a week for a three-week period were used for testing. It was observed that trackmen appeared to run better toward the end of the week than at the beginning, so a rotation of methods of warming-up was used. For example, the first week the subject would receive digital stroking before his performance on the first test day, on the second day he would receive deep massage, and on the third test day he would use exercises. The methods of warming-up were then rotated, so that on the first test day of the second week the subject would receive deep massage; the second test day, exercises; and the third test day, digital stroking. The third week the methods were rotated one step more, with the subject receiving preliminary exercises the first test day, digital stroking the second test day, and deep massage the third test day. All methods of warming-up were used on each test day in order to minimize the effect of such uncontrollable variables as the condition of the track and the effect of the wind. Thus, some subjects were given digital stroking, some were given deep massage, and some were given exercises on the same test day.

Results.—It can be seen in the table that there was no statistically significant difference in the running times after deep massage, preliminary exercises, and digital stroking. Since the difference in times was not statistically significant, the psychological effect of massage was not discernible.

Second Experiment

Because the results obtained in the first experiment showed that performances were equally good after deep massage, preliminary exercises, and digital stroking, the second experiment was conducted to compare the running time after digital stroking with that of a "cold run," when no preliminary warming-up was used.

Effect of Various Methods of Warming-Up on the Time of Running a Distance of 440 Yd.

Method of Warming-Up	Mean, Sec.	Standard Error, Mean	Standard Deviation	t-Ratio
Deep massage	55.6	1.53	4.05	0.48*
Digital stroking control	56.6	1.41	3.74	
Preliminary exercise	56.0	1.38	3.65	0.28*

* The differences in performance are not statistically significant.

Procedure.—Five highly trained varsity and freshmen track athletes of Springfield College were used as subjects. Each subject was tested four times, twice without warming-up and twice after digital stroking. The activity selected for testing was the 440-yd. run on an indoor track. As in the first experiment, digital stroking was used in order to detect any possible psychological effect of massage.

Results.—The average running time when no preliminary warming-up was used was 59.2 seconds, while the average time attained after digital stroking was 59.5 seconds. The computation of the *t*-ratio indicates that the difference between the effects of these two methods is not significant. The results may also be interpreted to mean that, whatever the psychological effect of digital stroking could be, it did not affect the running times.

Third Experiment

From the results of the first and second experiments, it was concluded that neither massage nor preliminary exercise improved the time of running 440 yd. Our conclusion that massage had no beneficial effect substantiated the findings of Asmussen and Bøje. However, the finding of lack of improvement after preliminary exercise, which is contrary to the findings of the previous investigations, made it necessary to study once again the effect of preliminary exercise upon performance. Since the only activity engaged in by the subjects was walking to and from classes and from the last class to the test, the question arose as to whether this walking was sufficient to substantially raise muscle temperature.

Procedure.—Warming-up prior to the performance consisted of riding the bicycle ergometer at a speed of 60 pedal revolutions per minute for five minutes with a load of 5.5 lb. On days the subjects rode without warming-up, they reported to the laboratory and without any preliminary warming-up they were given their test rides. No subject had been engaged in any physical activity for at least two hours before the test rides except walking to and from classes. The test rides were the same as the sprint performances used by Asmussen and Bøje, which they assumed to be equivalent to the 100-m. run. Each ride consisted of completing 35 pedal revolutions in the shortest possible time, the amount of work done being 956 kg.-m.

The three Springfield College students who were used as subjects were all excellently trained for this experiment, since they had just completed riding the bicycle ergometer for another study that had continued for several months. Twenty-four test rides were made: 12 after preliminary warming-up and 12 without preliminary warming-up.

Results.—The average time for the sprint rides without preliminary warming-up was 14.2 seconds, and that with preliminary warming-up was 13.7 seconds. Computation of the t-ratio showed that the warming-up did not have a significant beneficial effect on sprint rides on the bicycle ergometer.

Comment

If the interpretation of the obtained data were made on the basis of mean time of performance, it would have appeared that deep massage and preliminary exercise have a beneficial effect upon performance. A statistical analysis of the difference in time, however, showed that it was not significant and fell within the limits of experimental error.

The muscle temperature of men in the third experiment was 36.4 to 37.0 C (97.5 to 98.6 F) in cold state and 37.6 to 38.4 C (99.7 to 101.1 F) after warming-up. Therefore, a similarity between performance time with and without preliminary exercise cannot be explained by assuming that subjects who were scheduled to have a cold run warmed up by walking to the laboratory.

The running times recorded during the tests indicated that all subjects exerted maximum effort. In the experiment on the outdoor track, two of the subjects ran their fastest time of the track season. Both these performances occurred after warming-up by deep massage. One of the subjects in the second experiment surpassed the Springfield College indoor track record for the 440-yd. run. He ran without any preliminary warming-up.

Summary and Conclusions

Three series of experiments were conducted to determine the effect of warming-up upon physical performance. In the first experiment, seven trackmen ran 440 yd. after deep massage, exercises, or digital stroking. Digital stroking was used as the control and to study possible psychological effects of massage. In the second experiment, five men ran 440 yd. without warming-up and after digital stroking. In the third experiment, sprint rides on the bicycle ergometer after preliminary exercises and without warming-up were compared.

The experiments showed that deep massage, digital stroking, and preliminary exercise did not improve the time of running a distance of 440 yd. They also indicated that there was no beneficial psychological effect from massage. Finally, preliminary exercise did not improve sprint performance on the bicycle ergometer.

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Radioautography.—The term radioautography denotes a method of studying the distribution of radioisotopes which have become incorporated in an organism by observing the patterns created when the radiation from the isotope impinges upon a photographic film placed near the tissues. Radioautography is superior to the counting methods for some types of biomedical research with radioisotopes. For instance, accurate determinations of the sites of deposition of isotopes in organs and tissues (and in special cases in individual cells) can be made by means of radioautography. It is also possible to estimate the relative quantities of radioisotope in the various parts of a tissue. Occasionally, amounts of radioisotopes which will barely record on a counter will yield useful information by radioautography since the photographic film can integrate the radiation dose over a much longer time than is practical with Geiger-Mueller or scintillation counting. Furthermore, accurate counting radioisotopes in tissues requires the destruction of the tissue either by ashing, dissolving in acid or alkali, or homogenizing. This is not necessary with radioautography where the tissue, or at least the histological slide, remains intact and may be correlated with the pattern of the radioautogram. Several variations of the techniques of radioautography have evolved—such as: placing a photographic film (with its backing) in apposition with an histologic slide, floating the film (free of its backing) onto the tissue, mounting the tissue directly on a cut film instead of a slide, painting the melted film emulsion over the tissue on a slide, as well as others, and combinations of those stated. . . . In preparing the tissue slides for radioautography the chemical state of the isotope being used in the study determines the methods used for fixation and staining. Many of the reagents used in fixation, embedding, and staining may mobilize the isotope under investigation, removing it partially or entirely or causing it to diffuse more or less uniformly through the tissue. . . . In setting up new work it is well to monitor the various reagents through which the tissues are processed. If it appears that significant amounts of isotope remain in the reagents the method should be changed. All manipulations of the tissue should be such that the isotope is retained in its original positions.—D. Joftes and S. Warren, M.D., Simplified Liquid Emulsion Radioautography, *Journal of the Biological Photographic Association,* November, 1955.

NUTRITION AND ATHLETIC PERFORMANCE

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• *The performance of an athlete can be impaired significantly by a faulty or inadequate diet, even before clinical signs of a deficiency are manifest. But the manipulation of an already adequate diet does not enhance performance. The composition of a meal preceding single-effort events like the high jump has little effect on performance, but performance in tests involving prolonged muscular work is enhanced if carbohydrate stores are replete at the beginning of the test. Obesity is a mechanical handicap in most, though not in all, forms of athletics. The average corporeal density of athletes is higher than that assumed for the general population; therefore the usual height-weight tables give the misleading impression that an athlete of given height is too heavy and presumably obese. Placing him on a reducing diet would be a mistake. Ordinarily he will spontaneously ingest food in amounts sufficient to maintain his weight. Performance is generally influenced by motivation, skill, and other neuromuscular and psychological factors. The training table provides the athlete with the foods on which he has learned he can rely; it also provides some of the sense of security generally obtainable by the practice of rituals. The best diet for him is a balanced one consisting of a variety of the foods he enjoys, in amounts that maintain his weight at an optimum level.*

Manipulation of the diet in order to enhance physical performance is a procedure that has its roots in the superstition and magic of the unrecorded past. At one time, men swallowed powdered lion's teeth to make them strong. Similar practices are still carried on in primitive cultures. For many centuries the popular belief existed that violent muscular exercise requires the eating of a large amount of meat, and in the 19th century Liebig gave scientific support to this tenet by proposing that during exercise the substance of the muscles is used up. He stated, "All experience proves that this conversion of living muscular substance into compounds destitute of vitality is accelerated or retarded according to the amount of force employed to produce motion." Subsequent experiments showed conclusively that heavy exercise is not associated with any significant increase in loss of nitrogenous material; however, the conviction that meat was the food par excellence of the athlete was so strong, and the prestige of Liebig so great, that a number of years passed before the doctrine of "meat for muscular work" was reluctantly discarded.

According to Drummond and Wilbraham, concern for the diet of athletes paralleled the growing interest sport that began to be apparent in England toward he end of the 18th century. Early in the 19th century, it was customary for the athlete to begin his training with a series of strong purges to clear away "all the noxious matter he may have had in his stomach and intestines." After this "purification," unseasoned red meat (preferably underdone), bread, and mild beer were prescribed. Drummond and Wilbraham have written:

> The Oxford crew in the 'sixties trained on a diet of underdone beef or mutton, bread, tea and beer, with a little jelly or water cress as a treat at the evening meal. Instructions were given that no vegetables were to be eaten. Cambridge, on the other hand, suffered no restrictions regarding potatoes, greens, or even fruit. From 1861 to 1869 there was an unbroken succession of Oxford victories. So much for vitamins in athletics!

It is convenient to consider the effect of diet on physical performance at two levels: psychological and physiological.

Psychological Considerations

Much still needs to be learned about the effect of the psychological state of the athlete upon his performance. Yet, it is widely agreed that motivation plays a major part in determining whether an athlete will win a contest. The food that is consumed during training and immediately before an athletic contest may have a psychological significance for the athlete that exceeds its physiological and metabolic importance. The significance of eating rare meat as a symbol of manly vigor and strength is obvious. In the course of his training program, the athlete frequently must work hard and forego many pleasures. Accordingly, his need for gratification is accentuated. Some of this need can be met by providing him with appetizing foods, such as special desserts and rare beef. This provision makes him feel that training has its incidental rewards and helps to prevent him from "going stale." Presumably, there is an element of atavism in the emphasis on eating meat at the training table.

The drinking of milk (although not always recommended at the training table) has in some cultures become associated with the idea of health and "clean living." Then, too, the training table may provide some of the sense of security and reassurance generally obtainable by the practice of rituals. Use of various rituals by athletes in preparing themselves emotionally for contests is well known. Thus, food has a significance far beyond the nutrients it provides. Also, the atmosphere in which food is served is frequently more important than the quality of the food served. The morale value of turkey at Thanksgiving has been recognized by the military services, and on this holiday American soldiers stationed in far-off lands are served turkey, regardless of the cost involved.

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A number of studies have purported to show that between-meal feedings during working hours improve the efficiency of performance of industrial workers. However, when such studies have been repeated with use of suitable controls, it has usually been possible to demonstrate that the beneficial effects were psychological rather than physiological in origin. When ingestion of sugar before an athletic performance seems to have a salutory effect, it is difficult to decide whether this response occurs for psychological or physiological reasons.

In view of the importance of psychological factors in modifying physical performance, it would be unwise and unjustified to deprecate the psychological value of food, and of the ritual of the training table for the well-being of the athlete. However, it seems important to study these psychological aspects of food and the training table carefully in order that their contribution may be better assessed and clearly distinguished from possible physiological and metabolic factors.

Physiological and Metabolic Considerations

Digestion and Athletic Performance.—Considerable attention has been paid to the pregame or preevent meal. As Bensley has pointed out, the chief consideration to be borne in mind in planning this meal is the emotional stress that the athlete may experience on the day of the contest. Loss of appetite, abdominal discomfort, and even nausea, vomiting, or diarrhea may occur. If the meal is taken too close to the game or event, the anxiety of the athlete may interfere with appetite and digestion. Moreover, the distended stomach may impair performance. Therefore, in most cases, the preevent meal should be consumed not less than three hours before the contest. Individual food preferences should be respected. The athlete knows from experience which foods can be eaten without causing him discomfort. As a general rule, only foods known to be highly digestible should be consumed as part of the preevent meal.

Sources of Energy During Athletic Activity.—It is clear that variations in the normal diet cannot significantly influence the coordination and controlled expenditure of energy required in an athletic performance. These are matters of endowment and training. Conceivably, changes in diet may affect the amount of energy and the rate at which this can be made available. Obviously, an enormous variation exists in the expenditure of energy by athletes, and many classifications have been used to divide athletic performances in terms of energy expenditure. One such classification distinguishes four groups: (1) single-effort field events, such as the high jump, the broad jump, putting the shot, and pole vaulting; (2) sprints and hurdle races; (3) middle-distance runs, such as the mile run; and (4) prolonged efforts taking more than one hour, as exemplified by the marathon.

From what is known about intermediary metabolism, it would appear that the sources of energy for these classes of endeavor may be somewhat different. For example, in the single-effort events and sprints requiring bursts of effort, the body can make use of stored energy readily available from the energy-rich organic phosphates, adenosine triphosphate, and creatine phosphate. However, in order for the high-energy phosphate bonds of these compounds to be regenerated, fuel must be metabolized. To a limited extent, energy-rich phosphate bonds can be regenerated by the breakdown of glycogen to lactic acid, a process that does not require oxygen. However, the major supply of energy expended by the body is derived from the complete oxidation of small fragments derived from carbohydrate and fat. Indeed, per molecule of glucose, oxidative phosphorylation is much more effective than the phosphorylation connected with lactic acid formation.

In the 100-yd. dash, the oxygen requirement is over 6 liters. Since the human respiratory and circulatory equipment can provide only approximately 4 liters of oxygen per minute, it is clear that muscles are able to perform work and replenish energy stores for a limited time in the absence of oxygen. This is accomplished primarily by the breakdown of glycogen to lactic acid. However, this process is self-limited, since under such circumstances high-energy phosphate bonds are not regenerated as rapidly as they are broken down. Moreover, an accumulation of lactic acid in the blood occurs as a consequence of massive anaerobic glycolysis, and before long the products of the reaction, glycogen → lactic acid, accumulate to a point where the reaction itself can no longer proceed. Lactacidemia also may unfavorably affect blood acid-base balance and, consequently, the metabolic and physiological functions that depend on the maintenance of pH level within a certain optimal range. The oxygen needed to make up the energy deficit incurred during muscular exertion in the absence of adequate oxygen intake has been termed the oxygen debt. Not all of the oxygen debt is associated with lactic acid production: the balance ("alactacid" oxygen debt) may be used to restore creatine phosphate and adenosine triphosphate levels, and possibly to metabolize accumulated ketone bodies.

During the recovery phase, oxygen in excess of current needs is taken in to make up this deficit, which may be as high as 16 liters. In large part, the extra oxygen is used to oxidize the lactic acid accumulated during the deficit period. Such an oxygen debt can be incurred rapidly or more slowly. In practical terms, if an athlete exercises to a degree so that he needs 8 liters of oxygen per minute, he can maintain such a pace for only approximately four minutes, since in that time he will have reached the oxygen debt "ceiling" of about 16 liters. Since the oxygen requirement increases rapidly with an increase in running speed, the ability of the sprinter to achieve a pace almost 50% faster than that of the mile runner becomes readily explicable in physiological terms.

It must be emphasized that the body is not able to maintain an intake of 4 liters of oxygen per minute for very long. If exercise has to be maintained for a matter of hours, oxygen consumption approaches one liter per minute. Thus, as the energy expenditure of the athlete becomes more prolonged, its intensity must diminish. As its intensity lessens, the relative importance of the oxygen debt mechanism also diminishes. For moderate distances, the runner may depend in part on his "recovery" period; for long distances, he must run in a "steady state" (the condition in which the intake of oxygen meets the metabolic needs of muscle).

It would seem that, in the first three classes of athletic events listed above, the fuel supply is an item of minor concern, since the amounts of energy used are relatively small. In the fourth class, where endurance may be a deciding factor, the fuel supply becomes relatively more important. In any event, since diet does more than merely provide fuel for muscular activity, a more detailed analysis of the ways in which diet can influence performance is appropriate. Before such an analysis can be undertaken, however, the methods and criteria used in the assessment of physical performance should be briefly considered.

Influence of Diet on Physical Performance.—It has already been mentioned that motivation, skill, and coordination play important roles in determining the outcome of athletic contests. Thus, it is inherently difficult to study the problem of diet in relation to performance under satisfactorily controlled conditions. As Marrack has stated, "Excellence in athletics does not depend so much on the energy output by muscles and the rate at which this output can be maintained as on the skill with which this energy is used." Use of studies with animals in assessing the effect of diet on performance is not a particularly helpful procedure because of the difficulty in interpreting in human terms quantitative changes that may be measured in experimental animals. Keys has properly stressed the importance of using rigid standardization and has criticized many earlier studies because they were not sufficiently prolonged to eliminate the period of adaptation to a new dietary pattern suddenly imposed on the experimental subject.

Generally, the criteria used involve measurement of performance of an actual physical task, such as swimming 100 yd. or running a mile. The responses of such physiological factors as pulse rate, body temperature, and time of reaction to muscular activity also serve as indication of the ability to perform under standard conditions. Biochemical changes in the blood, particularly variations in values of blood glucose, lactic acid, and ketone bodies, have been measured during and after a standard task and used as indexes of performance.

The term "efficiency" applied to muscular activity is a technical expression that refers to the energy cost of mechanical work. Ordinarily, efficiency is calculated in one of two ways: as gross efficiency (total energy output in relation to mechanical work done) or as net efficiency (the increment of energy output over some predetermined base-line energy output, such as the resting or the basal metabolic rate, in relation to mechanical work performed). Gemmill has discussed the merits and disadvantages of such calculations in a comprehensive review. Of numerous methods for measuring the mechanical energy developed by man during exercise, the most commonly used is the bicycle ergograph. Considered as a machine, man operates at a maximal efficiency of about 25% (calculated for climbing stairs); this is somewhat better than the ordinary gasoline engine but not as good as the diesel engine.

In his review of the problem of physical performance in relation to diet, Keys has listed three ways in which special dietaries might influence muscular performance. These involve (1) renewing the supply of energy-yielding nutrients, (2) facilitating the energy-yielding reactions, and (3) counteracting physical-chemical changes in the body identified with fatigue. A fourth way in which diet can favorably influence physical performance is by reducing any appreciable excess in fat content of the body. Such a decrease in adiposity will result in a proportional decrease in the energy cost of moving the body or its parts.

The first of these categories has to do with the fuels of muscular exercise—carbohydrate, fat, and, to a lesser extent, protein. Because vitamins are essential constituents of enzyme systems, which, in turn, are an important part of the machinery of energy metabolism, these nutrients properly fall into the second category, which is concerned with the problem of facilitating the energy-yielding reactions. Since fatigue is believed to be a manifestation of altered physiology induced by excessive muscular work, the influence of muscular work on homeostasis can be considered in the third category. Lastly, since excess fat results from a positive energy balance maintained for a prolonged period, the problem of reducing the athlete's weight must be thought of in terms of the caloric provision at the training table measured against the day-by-day energy expenditure calculated for that particular person. Moreover, in athletes, obesity (or its absence) is frequently not diagnosed by the simple measurements of body weight and stature. There is good evidence that the caloric status of the athlete is best demonstrated by a consideration of his bodily composition. (Although clinical deficiency states obviously can be associated with impaired performance, such disorders have been excluded from consideration in this paper. The present discussion is concerned primarily with the problem of determining whether there is such a thing as an optimal diet for a given category of athletic performance.)

Carbohydrate: Most observers have noted that, when carbohydrate is readily available to tissues, it is used preferentially for muscular work. However, as reserves of carbohydrate diminish, increasingly more fat is metabolized. Accordingly, either carbohydrate or fat, or any combination of the two substrates, can provide fuel for muscular exercise. Krogh and Lindhard reported that, when subjects are on a high-carbohydrate diet, they show a higher net muscular efficiency than when they are on a high-fat–low-carbohydrate diet. Calculations based on respiratory calorimetry indicated that up to 9% greater expenditure of energy per unit of work occurs when fat is being burned (the respiratory quotient equals 0.7). The findings of Krogh and Lindhard were continued and confirmed in their laboratory by Bierring. However, as Gemmill has pointed out, these authors used a projected line to obtain the two extremes for their calculations. As actually determined, the highest respiratory quotient obtained was 0.93, when the work expenditure was 4.6 calories; the lowest respiratory quotient was 0.75, when the caloric output was 4.82. Accordingly, the actual difference between these two measured points is 4.5%. March and Murlin were unable to distinguish any relation between efficiency and relative quantity of fat and carbohydrate in the diet when light work was performed but noted a decrease in efficiency on a diet high in fat after such a diet was continued for three or four days.

Haggard and Greenberg performed studies with the bicycle ergograph that led them to believe that a high carbohydrate intake increased muscular efficiency markedly and that an increase in the interval between meals was associated with a reduced efficiency. Other investigators have been unable to discover a beneficial effect of carbohydrate on performance. After reviewing the literature up to 1942 on the subject of the effect on efficiency of diets high in carbohydrate or fat, Gemmill concluded that muscular efficiency is practically the same on all diets. He states that there is a slight increase in efficiency after a high-carbohydrate diet; which probably does not exceed 5%.

In prolonged physical activity, a definite correlation can be observed between symptoms of fatigue and a decrease in blood sugar level. When glucose is administered under these circumstances, the symptoms disappear and the power to work is increased. Christensen and associates believe that the beneficial effect of administered glucose is a neurophysiological phenomenon and not due to a direct metabolic effect on muscle. Apparently the respiratory quotient can continue to fall (indicating increasing oxidation of fat) even while the level of blood glucose is rising and the symptoms of fatigue are being alleviated. In subjects studied for relatively short periods, Simonson and co-workers were unable to correlate visual fatigue with changes in blood sugar level. Apparently, fatigue is not necessarily accompanied by hypoglycemia, although hypoglycemia is frequently accompanied by fatigue.

Considerable literature has appeared concerning the effect of breakfast and its composition upon performance of work and emotional status. Tuttle and associates found that omission of breakfast affected adversely performance on the bicycle ergograph. Thorn, Quimby, and Clinton and others have observed that a breakfast high in protein has value in maintaining the blood glucose level and also a feeling of well-being. Yet, many of the effects of omission of a meal may result primarily from the sudden interruption of an established eating pattern. Studies on individuals who habitually omit breakfast might be more rewarding. Moreover, it would be inappropriate to apply results obtained in studies on industrial or clerical workers to athletic performances. Before an athletic event, the athlete may be in a psychological and physiological state not at all comparable to what might be anticipated under more casual circumstances.

Concerning dietary sugar and performance, the remarks of Abrahams seem pertinent.

> What of sugar, approbated as a readily available source of energy to be taken before a contest? It is conceivable that in a very protracted effort the reservoirs might be exhausted and hypoglycemia occur. But that a special sort of explosive material can be advantageously applied for a maximum effort I do not believe. It is perfectly true that I have given sugar with results that encourage the men to accord no little credit to its service. But the highly strung athlete is so suggestible that he will be powerfully influenced by anybody in whom he has confidence, in which case it is immaterial what he is given. I have been convinced of this psychological element with substances simpler than sugar and sometimes quite inert.

Haldi and co-workers have studied the effect of carbohydrate intake on physical performance, using the time taken to complete a 100-yd. swim as the index. When a high-carbohydrate meal was taken three hours before the swim, performance was not better than that after an isocaloric meal low in carbohydrate. Blood sugar concentrations were higher after a swim of this distance in all cases but were not affected by the composition of the preswim meal. Haldi and associates concluded that, in brief periods of very strenuous exercise, muscular efficiency is dependent upon the energy reserves and the training of the subject. The composition and size of the preexercise meal do not appear to play a significant role.

Although the preponderance of available evidence indicates that the composition of the preexercise meal does not affect efficiency during athletic events of brief duration, there appears to be little doubt that the capacity to endure prolonged muscular work is enhanced if carbohydrate stores are replete prior to the exercise period. Whether this favorable effect is due entirely to the maintenance of higher blood glucose levels or whether it can be explained in part by the slightly greater efficiency of muscular work when carbohydrate is the predominant fuel is not entirely clear. Christensen and others believe that, in the last few days before an athletic contest, heavy work should be avoided to allow for maximal filling of carbohydrate stores. However, more experimental work is needed before it can be stated with assurance that this belief is well founded.

Fat: There is no doubt that fat provides fuel for muscular work. In sustained exercise, when carbohydrate reserves diminish, the respiratory quotient falls, indicating that an increasing proportion of fat is being oxidized. However, fat seems to play a passive role in energy metabolism, in the sense that, when carbohydrate is available as a fuel for exercise, the respiratory quotient usually rises and the contribution of fat to energy metabolism diminishes in proportion. When exercise ceases, the respiratory quotient again falls to low levels, indicating that the metabolic mixture in the blood is largely composed of fat. In the diet of athletes (as in general), fat, at the metabolic level, acts as an indifferent source of energy. Beyond this, it makes no special contribution to muscular performance.

Protein: Since Zuntz and others have shown that protein is not metabolized in significant amounts during muscular exercise in the well-nourished person, it need be considered only briefly, as having an energy-releasing reaction. The importance of meat as a constituent of the diet of athletes has been much debated, but it would appear that an excess of meat at the training table probably has more psychological than physiological value. The requirement for protein is not significantly increased when exercise is performed, unless at the same time an increase in muscle mass is taking place.

Yamaji carefully studied protein metabolism in several students who were being subjected to a rigorous training program for approximately one month. He observed that as the training progressed the nitrogen balance became positive. When the regular diet, containing 1 to 1.5 gm. per kilogram of body weight of protein per day, was fed, retention of nitrogen was relatively small; however, when the protein content of the diet was increased to 2 gm. or more per kilogram of body weight per day, an increasing amount of nitrogen was retained. This investigator also followed changes in the reserve protein during training for heavy muscular work and found that early in training the hemoglobin and albumin contents of the blood decrease. The degree of decrease in these blood proteins and the rate of their recovery are apparently influenced by the amount of protein in the diet. The higher the dietary protein intake, the smaller is the decrease in hemoglobin and serum albumin levels at the beginning and the sooner the return to normal.

As a result of these findings, Yamaji has concluded that during training protein accumulates in muscles at the expense of blood proteins. He has recommended that, during training programs involving heavy muscular work, an excess of protein be consumed. Such a diet would help to prevent anemia and permit the muscle mass to increase in size more rapidly. If Yamaji's results can be confirmed, it would mean that hemoglobin synthesis does not necessarily take precedence over other protein requirements, as some studies have implied. In any event, it seems clear that determinations of nitrogen balance during periods of rigorous training indicate only whether a net catabolism or anabolism of protein is taking place.

Additional studies, including determination of body constituents, are needed to provide information about important internal changes in protein metabolism that may be taking place. The studies of Yamaji and his colleagues deserve to be carefully followed up in the United States, particularly with respect to changes in reserve or labile protein that may occur during conditioning periods in athletes who have been out of training for some time. If the athlete is a growing boy, he will need extra protein to meet this particular anabolic requirement, whether he is in training or not.

Vitamins: It is now widely recognized that many vitamins of the B group are important constituents of coenzymes that participate in the energy-releasing reactions for which carbohydrate and fat provide the major substrates. The specific vitamins known to be involved are thiamine (cocarboxylase), riboflavin (flavoprotein coenzymes), nicotinamide (diphosphopyridine nucleotide, or coenzyme 1, and triphosphopyridine nucleotide, or coenzyme 2), pantothenic acid (coenzyme A), and probably pyridoxine (codecarboxylase) and biotin (carbon dioxide—fixation coenzyme). The rationale for believing that vitamin supplements might significantly affect physical performance involves the assumption that subclinical vitamin deficiencies are not uncommon in apparently well-nourished persons or, failing this, that it is possible to supercharge the energy-producing reactions by providing an excess of vitamins.

Keys and his associates were unable to discover any benefit to performance of work or capacity from large daily supplements of the B vitamins given to soldiers maintained on ordinary U. S. Army garrison rations. In his review, Keys states that he has been unable to find convincing evidence that supplements of the B complex or vitamins C or E, separately or in combination, would enhance the physical performance of apparently well-nourished persons. Bourne has recommended a high vitamin intake for athletes on the ground that the requirement for certain vitamins may be enormously increased in strenuous exercise. Actually, there is very little evidence to suggest that the requirement for vitamins is appreciably increased during prolonged muscular work. At best, the requirement for certain vitamins may increase in direct arithmetic proportion to the increase in expenditure of energy. In spite of occasional reports of apparently beneficial effects of vitamin supplementation upon athletic performance, it remains to be demonstrated convincingly that supplementation of the diet of the athlete in training with vitamins of any sort has a beneficial effect on endurance, muscular efficiency, or coordination.

Electrolytes and Blood Acid-Base Balance: After brief periods of strenuous exercise, there occurs a marked increase in production of lactic acid by the working muscles. At the same time a moderate increase in production of pyruvic acid takes place. These values are greatest 5 to 15 minutes after such exercise but remain comparatively high during the balance of the recovery period. According to Christensen and coworkers, the rise in lactic acid brought about by work of definite severity becomes less for the subject in better training. However, there is no evidence that the trained subject can dispose of excess lactate more rapidly than the untrained person.

The mechanism of lactacidemia has already been discussed. However, since severe exercise is associated with an accumulation of large quantities of organic acids, alkalinizing procedures have been suggested as having possible value in relieving the fatigue of the athlete. Johnson and associates studied the effects of blood alkalinizers on the efficiency of runners and found that their running times were not shortened by such measures. Keys has concluded tentatively that such changes in the alkaline reserve that may be effected by dietary manipulation will have little influence on the ability of the normal person to perform muscular work.

When carbohydrate stores are depleted during prolonged strenuous exercise, a rise in blood level of ketones may be anticipated. According to Grollman and Phillips, the degree of ketonemia occurring under controlled dietary conditions during performance of a standard task involving muscular exertion varies directly with the degree of training of the individual performing the task. They postulate that the greater rise in levels of blood ketones in the trained individual may represent a more efficient pathway for fat metabolism under these circumstances. Grollman and Phillips also have suggested that accumulated ketone bodies may represent that portion of the oxygen debt not accounted for by lactacidemia. Incidentally, there appears to be no evidence that the mild to moderate ketonemia of exercise during a time of carbohydrate depletion is in any way deleterious.

Frequently, athletic contests are carried on during hot weather and are associated with excessive losses of sodium chloride and water from the skin. Obviously, under these circumstances, replacement of salt and water is needed. Keys and associates have found that work capacity in heat is markedly reduced when salt is severely restricted, even when this does not involve heat cramps or heat hyperpyrexia. At least 2 to 3 gm. of sodium chloride must be replaced per liter of sweat lost. Salt tablets may be upsetting to the digestive tract, and many physicians have found a weak solution of sodium chloride to be better tolerated by the individual deficient in salt.

Calories and Body Weight: Ordinarily, the athlete will spontaneously ingest food in amounts adequate to maintain his weight. It is unusual for obesity to develop during a period of rigorous physical conditioning; however, if the training-table food is appetizing and also calorically concentrated and the training itself moderate, it is quite possible for the athlete to accumulate fat during the training period. If the athlete has allowed himself to gain fat intercurrently, he will tend to lose it during the training period. It is axiomatic that the athlete who decreases his total weight by losing excess fat will be a more efficient machine. Accordingly, for most forms of athletics, obesity, even to a mild degree, constitutes a mechanical handicap.

The development in Germany of a light, portable respirometer has made possible the convenient collection of fairly accurate information about the caloric cost of different kinds of athletic activity. In assessing the nutritional needs of athletes, it is clearly important to obtain reliable information about the calories expended by the athlete in the performance of his particular event or events. Passmore and Durnin have carefully reviewed much of the recent information on the subject of expenditure of energy of man. They have recorded figures for the energy costs of different sports expressed as calories per minute. For example, they note that skiing at moderate speed on level, hard snow involves a significantly greater energy cost than swimming the crawl at a rate of 55 yd. per minute. On the basis of quantitative information of this sort, it should be possible to obtain a better understanding of the caloric needs associated with a variety of sports.

As a result of application of dilution and densitometric methods, considerable information has been gathered concerning the body composition of athletes. Welham and Behnke studied 25 athletes and found that, on the basis of standard height-weight tables of the type used by the insurance companies and the military services, 17 fell into the overweight category. When these investigators performed determinations of specific gravity on the 17 subjects who, by conventional standards, would have been classified as obese, they discovered that 11 of the group possessed high corporeal specific gravity. This indicated that these particular "overweight" subjects actually had a relatively low content of body fat and a proportionately increased lean body mass. On the basis of these findings, the authors have proposed that overweight should be defined in terms of the specific gravity of the body mass, with a tentative dividing line at the value 1.060 (specific gravity) between the obese and nonobese categories.

If the conventional criterion of desirable weight, based on relationship between height and weight (modified by age), is used uncritically as a guide, it is conceivable that a number of lean athletes might be placed on reducing diets in the mistaken belief that they were obese. Such a procedure could only impair the athletes' ability to perform. Thus, in the assessment of the caloric status of athletes, it would seem particularly important to use criteria supplementary to the simple determination of body weight, such as the difference between circumferential measurement of chest and abdomen and the measurement of thickness of skin fold with appropriate calipers.

Summary

Ability to perform well in an athletic event depends primarily upon the skilled and coordinated use of a well-endowed and properly conditioned body; however, psychological factors such as motivation may be important in determining whether the athlete will win or lose a contest. Awareness on the part of the athlete of having regularly consumed an appetizing diet of wholesome foods at the training table is one of a number of factors that can have a favorable effect on his morale. A preevent supplement or meal taken in the belief that it will provide extra energy and thereby enhance performance also may have a beneficial psychological effect. Therefore, by affecting the psychology of the athlete, the training diet and the preevent meal can affect his performance. Since the athlete frequently experiences considerable nervous tension (with its digestive consequences) on the day of a contest, the preevent meal should consist of tried and true foods of a highly digestible nature taken some three or four hours prior to the event.

There is no evidence that the diet immediately prior to a short-term athletic event can be manipulated in such a way as to improve performance. In longer events requiring sustained muscular work, there is considerable drain upon the carbohydrate stores and a falling blood glucose level may be associated with marked fatigue. Accordingly, the degree to which carbohydrate stores are filled may affect endurance. A small increase in muscular efficiency is believed by some investigators to occur when carbohydrate rather than fat is the predominant fuel for muscular work. Whether such an increased efficiency can significantly influence athletic performance remains to be determined. In any event, it seems desirable to prepare athletes participating in contests requiring endurance with diets that will ensure maximal filling of carbohydrate stores prior to the event.

The trained athlete requires no extra protein; however, there is evidence that during rigorous training the diet should contain liberal quantities of protein in order to permit the muscle mass to increase rapidly and without cost to labile protein sources elsewhere in the body. Supplementary vitamins probably are not needed in the nutritional program of the athlete who is consuming a nutritious diet. A slight sodium deficiency can impair athletic performance before any clinical signs of sodium lack are discernible. There-

fore, during hot weather, adequate amounts of salt and water should be given to replace losses of these substances through the skin. Excess body fat can be an important mechanical handicap for the athlete; yet, caution must be exercised in diagnosing obesity in the athlete who is merely overweight in terms of the standard height-weight tables. Many "overweight" athletes are not actually obese and, for this reason, more informative measurements than those of weight and stature should be made when the athlete's caloric status is being assessed.

Although there is considerable doubt whether manipulation of an adequate diet can enhance performance, there is no doubt whatever that performance can be significantly impaired when a less than adequate diet is consumed. The best diet for the athlete is one he enjoys and one that, at the same time, provides a variety of nutritious foods in amounts adequate to maintain his weight at an optimal level.

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Because of space limitations, a bibliography has been omitted from THE JOURNAL and will appear in the authors' reprints.

PREVENTION OF INJURY IN ATHLETICS

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• During the 1955 football season, nine deaths were recorded throughout the course of play. This alone shows the need for an active program concerning the prevention of athletic injuries. As a prerequisite to such a program, accurate statistics must be obtained to show types of injuries and rate per exposure for all sports.

A preventive program must include a thorough preseason physical examination, with special emphasis on the history of prior injuries that the examinee might try to hide. There should then follow a period of physical conditioning under close medical observation, no matter what the sport or competition. The physician's responsibility, after all means of prevention have been utilized, lies notably in the immediate diagnosis, treatment, and prognosis of injuries sustained and in averting further aggravation of minor trauma. This is not the duty of the coach or trainer.

Closer medical supervision of athletics, perhaps with a program similar to that practiced by industry and the insurance companies for the protection of the worker, may be the means of reduction of athletic injuries.

Prevention of injury in industry has recently been brought to the attention of our reading public by James P. Mitchell, Secretary of Labor.[1] Information concerning the year 1955 reveals that on-the-job injuries and deaths involved 1,935,000 workers, with an economic loss calculated at 3.5 billion dollars. In spite of these appalling figures, we are informed that the disability injury rate per million hours worked has declined, from 20 in 1943 to 11.9 in 1954. In contrast with this organized effort of industry and of insurance companies to make all workers conscious of injury by specific training in accident prevention, one can observe little organized endeavor on the part of coaches, trainers, and others in the field of sports to institute training programs along the same lines. Sporadic changes in rules and regulations such as those pertaining to equipment and padding have partially benefited the safety of the game, but enforcement has been lax. Even the sports-loving spectator is stimulated to action when a good brawl is taking place on the ice or on the playing field. Of course, such brawls should not exist, according to the rules and regulations. "Baiting" the umpire by coach and/or player is often tolerated in our popular game of baseball.

Statistics on Injuries

Until such time as accurate statistical material concerning all sports and the number of regular participants is available, it will not be possible to ascertain the true incidence of injury per exposure in any one sport. Since 1931 the American Football Coaches Association[2] has made statistical reports on the fatalities of football. However, in this popular sport many disabilities occur that do not result in death but require treatment and absence from practice or games. A great need exists for an accurate tabulation on a national scale of all injuries resulting in disability for more than one day incurred in each sport. The problem of obtaining the necessary data for compilation is one of organization. Except for those of isolated educational institutions, such reports are now unobtainable. The American College Health Association, in cooperation with the National Safety Council, has attempted such a study but could obtain cooperation from only 11 colleges the first year and 9 the second year.[3] Reports in medical literature on the subject of athletic injuries are varied and usually concern particular types of injury. The information sought requires reports covering all professional sports and collegiate and high school athletics with formal, extramural competition. Basketball, baseball, football, soccer, lacrosse, boxing, and wrestling should be included in these reports. Such a large base for statistical compilation would furnish data of great value to those interested in the reduction of the incidence of injury in sports competition. I believe that the current incidence of injury is too high and should and can be reduced.

Need for Cooperative Effort

Our larger universities are interested in reducing the incidence of injuries in intercollegiate sports, as are the larger professional leagues in baseball, basketball, football, and ice hockey. However, due to a feeling of independence on the part of those in professional and amateur competition, too few have undertaken cooperative endeavor really aimed to benefit all competitors. Such an attitude has probably arisen as a result of the American definition of the amateur athlete. There has been much eyebrow-lifting over the international competition in the Winter Olympics in 1956, when those nations behind the Iron Curtain carried away most of the championships. Relying upon a fixed definition of qualifications for amateur competition, the Western sports world must examine its own code of amateurism. When does an athlete retain his true amateur status today? Whether amateur or professional, however, everyone interested in sports is interested in a program to reduce the incidence of injury and of fatality in sports. One is little cognizant of the facts. Is it realized that in the 1955 football season there were recorded nine deaths during play in American football and one death in the relatively harmless "touch" football?[2] In 1951 Gonzales[4] reported on deaths from sports; these data were derived from the files of the medical examiner's office in New York City covering 32 years, as follows: baseball, 43; football, 22; boxing, 21; and basketball, 7. Whatever program is adopted to reduce the incidence of injuries in sports will require deep thought and cooperation from all sides of the field: the professional, the amateur, the schools, and those responsible for sports in public and private playgrounds. The Metropolitan Life Insurance Company[5] has reported an astounding number of fatalities from sports injuries among its industrial policyholders, even in casual sports competition for fun (three fatalities in golf in two years). The medical interest in any program to prevent injury transcends any boundary, national or international, amateur or professional, sand-lot or organized.

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Program for Prevention

Any suggested program on prevention of sports injuries begins with the compulsory preseason physical examination of all competitors. The physical examinations and medical history should emphasize prior injury and its sequelae, if any; vision; teeth and dentures; the heart and cardiovascular system; the respiratory system; the excretory system; and the musculoskeletal system. The examiner should look for the presence of large postoperative scars or any congenital or acquired abnormalities. A history of prior sprain of a ligament, strain of a muscle or tendon, or fracture is of great importance. Protective strapping has been demonstrated as useful in reducing the incidence of recurrent sprains and strains.[6] Many eager competitors like to hide the earlier injury, and the examing physician must be alert to note anything of this nature at the earliest possible moment. Cerebral concussion is occurring more frequently in the medical histories of the entering freshman athletes. It is often the result of an automobile accident rather than an accident on the playing field. A history of multiple concussions in a would-be college athlete interested in body-contact sports, when there has been loss of consciousness on three occasions, in our code automatically prevents him from entering competition and necessitates a detailed examination and consultation with the neurosurgical consultant. When the above-described physical examination uncovers only a marked abnormality of vision, the services of a consultant in ophthalmology are required. When there is correctible defective vision, contact lenses are ideal for those who can tolerate the prosthesis during exercise. In my experience, only a small minority of athletes can be comfortably fitted. When the physical examination is completed by the physician, the findings are reviewed by a higher authority on the medical staff and a complete list of approved candidates forwarded to the team surgeon, the team manager, and the team coach. No unapproved candidate can obtain a uniform.

After his acceptance as physically fit for a sport, the candidate reports to the squad and comes under the surveillance of the coach and training personnel. The fundamental training period is vital to the development of talent and technical and physical skills in all team sports. Actually more than the development of skill and talent is achieved through practice and drill. A physical conditioning is derived. No matter what sport may be considered or what game is played, certain fundamentals are required—in the basic knowledge of the sport, in the more advanced plays, in defensive maneuvers, or in offensive chance plays by which a temporary advantage is seized to gain or to score. In addition to the technical knowledge of the game and its rules, the physical strength to outlast opponents has more than once proved the winning factor in many a close contest. The coach and the trainer sense the quality of physical fitness and team cohesion as any season of sport proceeds.

One of the most difficult factors to deal with in a squad is the problem of overtraining. This is largely a problem of individual reaction, and one key man in the team can slow or upset the entire squad. Overtraining is a contagious affair that seems to travel unnoticed by squad members at the time, but a keen coach with an eye to individual members of his squad can spot and call it. It is better described, perhaps, as an unrecognized attempt to perfect some technical maneuver of a game to too ultimate a goal. Try as one may, the goal becomes succeedingly more impossible. However, the solution to this problem lies in more natural attempts, without trying too hard. Overtraining is largely mental weariness. Regardless of what sport may be concerned, one sees this. It is a bugbear of the coaching staff that the more experienced recognize early. The great problem of the coaching staff of any team, whether professional or amateur, is to develop the squad through graduated physical exercise and gradual technical training in offensive and defensive play, so that at the climax of the season, whether the goal be a world championship or a league championship, the squad has progressed to meet the challenge all the way through the competitive schedule. In the various professional, intercollegiate conference, and other leagues, the nervous tension felt during the sports seasons has reached a high level that 50 years ago would have been inconceivable.

The coach and training staffs do contribute to the program for prevention of injuries by teaching applicable techniques, particularly those related to defensive play in competitive sports. A very important detail pertains to the perfection of timing of team play in body-contact sports, in both offensive and defensive maneuvers. Lack of perfection in timing can produce uncalled-for injury; lack of proper execution of a play by one member of the team may result in unintended exposure of a teammate to uncalculated risk; and, unless alertness by team members to this potential risk is emphasized during squad drill or practice, a major source of the incidence of injury has been overlooked. All good coaches appreciate the necessity of squad drills in timing in complicated offensive and defensive play in all body-contact sports.

Another factor must be considered in prevention: the medical staff's responsibility for early recognition of injury to a member of the squad. Much has been written on the importance of early recognition of injury, the prompt removal of the player from the game, and the application of therapeutic measures, so that a minor sprain or strain may not become a major disability. Since the coach's main interest is in the technical perfection of team and position play, he should not be required to spot a limping or arm-weary player. The problems pertaining to minor injury should be the responsibility of the medical observer. Those of us trained in the process of observation for such details can perfect our visual sense so as to spot the milder type of injury before the player himself exhibits the aggravated symptoms. Time out for examination often prevents a seriously disabling injury. However, the acceptance of such responsibility might bring an overbearing interference with squad training if reasonable restraint were not exercised.

As I have seen sprains unnecessarily produced because of certain irregularities in the playing surface, I wish to point out that this danger, particularly in sand-lot competition, has even resulted in fatalities. Improvement in the floor surface of the boxing ring, as a result of changes in rules, has reduced the number of head injuries incident to that sport. In the Eastwood report[2] of fatalities directly caused by football for the 1955 season, 20% were in sand-lot competition. Those responsible for maintenance of grounds must remain alert to the potential dangers of uneven playing surfaces.

Responsibility of Rules Committees and Officials

In October, 1955, the lay press[7] emphasized that the great American football game was developing into a game in which the protective equipment worn by the players might be becoming too heavy and/or too rigid. One could interpret this as suggesting that a player might use his equipment to take advantage of his opponent, offensively or defensively. There is no question that the intent in the designing and developing of new protective equipment is to protect the individual wearer against injury. The various sports rules committees have regulated the hardness of padding that may be worn over certain parts of the body and are always alert to legislate against a particular type of rigid padding used on a particular [illegible] body where it might be utilized as an offen[illegible] on. They act similarly with regard to station[illegible] ment. The rules of boxing were recently [illegible] require a new type of floor matting in the [illegible] which has materially altered the incidence [illegible] head injuries.[8]

Likewise, some years ago the American [illegible] rules committee moved the location of the [illegible] back 10 yards to avert possible injury to [illegible] However, in my opinion, the number of seri[illegible] injuries caused by impact against these [illegible] located on the goal line was not significant [illegible] fessional football in the United States and in [illegible] the posts are still maintained on the goal [illegible] ever, nobody can deny that all are interested [illegible] ing the incidence of injury from body contact. [illegible] taking research on the plastic football helmet [illegible] proper suspension is now being done at Corn[illegible] versity, Ithaca, N. Y., and the University of [illegible] California, Los Angeles. One hopefully looks [illegible] to the ideal design and a reduction in the [illegible] of cerebral concussion.

In body-contact sports today, more respo[illegible] has been placed on contest officials. In baseb[illegible] football the number of officials has been in[illegible] with the idea of better coverage of all facets [illegible] complicated, technical game. The rules and [illegible] tions of all games are complex, but those with [illegible] ber of players scattered over the field require [illegible] fields of vision than are needed in the boxing [illegible] tling ring. Nonenforcement of the rules of the [illegible] spoils the sport, and, in some sports, the sole [illegible] may have too great a responsibility. It is a [illegible] tragedy to report that in 1956, in a freshman pre[illegible] tory school wrestling bout in Springfield, Mass., [illegible] contestant sustained a fracture of the sixth cer[illegible] vertebra and a transected spinal cord. In interco[illegible] iate football too many fouls or infractions of the [illegible] seem to go unnoticed. It is distressing to see in [illegible] game so many instances of broken or displaced teeth [illegible] often occurring in line play. Perhaps the fault lies [illegible] the rules, but perhaps it is the laxity in officiating

TABLE 1.—*Incidence of Sprains and Length of Disability Incurred in Sports at Harvard University*

	Ankle Sprains, No.		Disability Days		Knee Sprains, No.		[illegible]	
Sport	1946-1947	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
Varsity football	7	2	[illegible]	[illegible]	4	5	31	[illegible]
Jr. varsity football	7	3	[illegible]	15	5	4	71	[illegible]
Intramural football	12	1	75	[illegible]	9	3	[illegible]	[illegible]
Totals	[illegible]	6	[illegible]	[illegible]	18	12	211	[illegible]
Av.			[illegible]	[illegible]			[illegible]	[illegible]

Physician's Responsibility

The purely medical prerogative is the diagno[illegible] treatment, and prognosis of all individual injuries [illegible] sustained. In addition, the prerogative pertaining [illegible] the prevention or aggravation of minor injury belo[illegible] to the medical staff. No one can deny that progress [illegible] been made in reducing the days of disability [illegible] athletic injuries. Table 1 demonstrates significa[illegible] the results of early, prompt treatment. Physicia[illegible] trainers, and coaches are all concerned with the individual player and his welfare. The permitting of a player with cerebral concussion to continue play should not be tolerated. Even the player who is exhausted physically and physiologically is more prone to injury if permitted to continue.

A player not mentally or physically capable of carrying out his assignments is of less value to a team than a fresh substitute. Every follower of body-contact sports can recall having seen some player allowed to continue in a rugged contest without full capacity of his mental processes. In the high school leagues particularly, there is lack of adequate medical supervision of practice sessions of contact sports. The responsibility lies in the community schools' committees. According to Eastwood's report[2] of the nine football fatalities in 1955 that were a direct result of competition, six were deaths of high school players. It is unfair to a coach not to provide him with adequate medical assistance. Even though the majority of injuries sustained are not serious, nobody can prophesy when a serious accident might occur.

The team physician must grasp the opportunity to determine whether a limping player should be taken out of competition. He should arrange with the team captain to call time out for any needed examination. He should be familiar with the functional testing of joints, the more common sites of fracture, and the simpler tests for diagnosis of type of injury. In instances of head injuries, he should be alert and ask the player simple questions in order to determine whether there is amnesia, with no orientation of time and place. If necessary the physician could call upon the team captain to interrogate the injured player in order to determine whether the player knew his particular assignment in an individual play signal. When an arm or leg is involved, comparative tests of the normal side and the injured side are simple and very practical.

TABLE 2.—*Types of Injuries Incurred Most Commonly in Sports at Harvard University*

Injury	1932-1937	1937-1942	1942-1947*	1947-1952	1952-1954	Totals
Sprains	636	426	210	344	86	1,702
Strains	363	287	96	145	53	944
Contusions, joint	219	73	87	52	17	448
Contusions, muscle	526	350	111	60	18	1,065
Contusions, simple	281	93	103	97	22	596
Fractures and dislocations	223	232	105	181	47	788
Lacerations and abrasions	264	89	25	40	6	424
Inflammations and infections	300	131	66	48	9	554
Internal injuries	102	91	39	115	26	363
Miscellaneous	243	152	67	42	6	510
Totals	3,157	1,914	909	1,124	290	7,391

* From fall, 1943, until spring, 1946, the sports were on a wartime basis, with organized sports continued only informally and on a limited scale.

Once the injury is located and diagnosed, its severity or degree is the important decision to make. Will continued play turn a sprain from grade 1 into grade 2 or grade 3? In many instances one cannot determine the degree of injury until 24 hours later. The player should be protected from a possibly long disability period. There is no reason, from the pathological point of view, to think that a sprained ligament can be supported by adhesive strapping, so that the player can be returned immediately to play, without doing irreparable harm to the injured ligament. The torn ligament must heal, and one cannot put stress on it until the healing process is complete, and then only with daily supportive adhesive strapping. It will never again be as strong, since there will be fibrous scarring. The too early return to play of a player with a healing sprained ligament can undo good results of the partial healing process. The team physician must determine when the lesion has healed and the player is ready to return to play. He must realize that, if a player still limps, an ankle sprain is incompletely healed and that, regardless of the amount of adhesive tape applied, the player cannot yet withstand the stress of running and dodging.

TABLE 3.—*Body Distribution of Injuries Incurred in Sports at Harvard University*

Region	1932-1937	1937-1942	1942-1947	1947-1954*	Totals
Abdomen	18	10	1	8	37
Achilles tendon	31	5	3	4	43
Ankles	344	200	125	226	895
Arms	38	35	12	15	100
Back	87	57	5	32	181
Buttocks	29	10	0	3	42
Calves	147	91	48	14	300
Chest	75	48	55	35	213
Crotch	27	0	0	1	28
Elbows	53	38	21	12	124
Face	228	122	44	48	442
Feet	187	68	39	45	339
Groins	114	108	39	21	282
Hands	288	109	55	41	493
Head	182	109	71	140	502
Heels	32	8	2	3	45
Hips	58	26	0	4	88
Knees	426	301	137	273	1,137
Iliac crest	30	29	24	28	111
Neck	20	14	1	11	46
Shins	54	16	7	60	137
Shoulders	212	189	64	129	594
Teeth	14	1	0	11	26
Thighs	416	240	113	142	911
Throat	11	6	6	15	38
Viscera	35	42	16	12	105
Wrists	51	32	21	31	135
Totals	3,267	1,914	909	1,364	7,394

* 7-yr. period; other periods are 5 yr.

Diagnosis and Treatment of Common Injuries

The team physician should become familiar with the more common types of injuries produced in athletics and likewise the more commonly injured parts of the body. Tables 2 and 3 illustrate my own experience. Alertness on the part of the trainer and team physician and recognition of the more serious and less common injuries is a "must" in organized sports. In most body-contact sports, there is a time limit of three minutes in which the one responsible for diagnosis and prognosis must decide whether an injury is of sufficient degree to require the player to leave the field.

Sprains, strains, and contusions account for over 60% of the injuries sustained in competitive athletics (table 2). A full knowledge and understanding of the pathology[9] of such lesions is necessary for all team physicians. Diagnosis and prompt institution of appropriate treatment are the key to a reduction in the

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STUDY OF THE LONGEVITY AND MORBIDITY OF COLLEGE ATHLETES

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• *When 629 athletes were compared with 583 nonathletes with approximately the same college environment, there appeared to be no significant difference in life expectancy, cause of death, or the type of death. The criterion of being called an athlete in this survey was to have been a varsity-letter winner. This particular study is in agreement with other recent studies of a similar nature.*

The effects of intensive athletic competition on the heart and other organs and on bodily resistance to disease has long been a subject of controversy. Previous to the work of Morgan [1] in 1873, the viewpoint prevailing in England was that competitive oarsmen did not live beyond 50 years of age and that this reduced longevity was directly caused by athletic competition. The studies of Morgan [1] and Meylan [2] in 1904 refuted this concept. Attempting to gain further insight into the longevity of athletes, Anderson [3] and Greenway and Hiscock [4] compared the longevity and causes of death of Yale University athletes with use of insurance tables. Dublin,[5] Knoll,[6] Hartley and Llewellyn,[7] and Wakefield [8] similarly compared their data on athletes with insurance company or general population statistics. Bickert,[9] Van Mervennée,[10] and Schmid [11] added to the body of information available on the longevity and morbidity of athletes but presented no control data. Hartley and Llewellyn [7] point out that athletes are a select group and that, therefore, comparisons with data of life insurance company tables are open to serious criticisms. Dublin [5] stated that a comparison of athletes with their classmates might yield more valid information.

Dublin's [12] second study in 1932 and Rook's [13] work in 1954 represent perhaps the best analyses in the literature on the longevity and causes of death among athletes and nonathletes. Dublin's results show the expectation of life in years at age 22 for honor men (47.73) to be greater than for either the average graduate (45.71) or the athlete (45.56). All college groups, however, showed greater life expectation at age 22 than was listed in tables covering the period 1900-1915 for American men (44.29) or was given for American white males listed in the 27 registration states of the United States for 1919-1920 (43.35). Rook's results as to longevity varied from Dublin's, in that the average age of sportsmen at death (67.97) exceeded that of the randomly selected group (67.43) in his study. The intellectual group again, however, had the greatest longevity (69.41). In all studies in which causes of death were investigated, deaths by external violence among athletes markedly exceeded those among controls. Typically, Wakefield [8] in 1944 found 34% of all deaths among former basketball players were due to external violence, as compared with 17.3% for the general population of the state of Indiana. Rook found the death rate due to external violence to be 97.9 per thousand for sportsmen, as compared with rates of 46.7 for intellectuals, and 70.4 for his random group.

The results of studies regarding comparative rates of death due to cardiovascular causes do not indicate clear trends. In Rook's [13] study for instance, 27.3% of the deaths before age 65 among controls were due to cardiovascular conditions, as compared to 22.5% among sportsmen. Wakefield's [8] results, on the other hand, showed 25% of all deaths caused by disease to be due to cardiovascular-renal diseases, as compared to only 16% for the general population of Indiana. Dublin's [5] results in 1928 showed that, of all deaths among athletes over 45 years of age, 32% were due to heart disease, as compared with a rate of about 20% of the total deaths among insured groups from this cause.

Present Study

The present study was undertaken as a pilot study of the larger national research project inaugurated in 1951 and sponsored by the physical education honorary fraternity, Phi Epsilon Kappa. Questionnaires prepared by a national study committee were sent out to 1,130 former athletes and 1,130 others not former athletes, individually matched as to years of attendance at Michigan State University and ranging in dates of birth from 1855 to 1919. (For purposes of this study, athlete is defined as a letter winner in a varsity sport.) Of the 2,260 questionnaires sent out, 1,212

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Read before the third Annual Convention of the American College of Sports Medicine, Chicago, April, 1956.

were returned with sufficient information to be included. Six hundred twenty-nine, or 55.66%, of the questionnaires sent to athletes were returned, as were 583, or 51.59%, of those sent to the control group. The distribution of returns by year of birth shown in figure 1 would seem to indicate that comparisons are justified with respect to longevity or causes of death. Data from the questionnaires were tabulated, punched onto IBM cards, and analyzed, insofar as possible by IBM techniques. The data have been statistically analyzed where appropriate (tables 1 and 2). One hundred twenty-three, or 9.85%, of the total returned questionnaires were for deceased subjects, of whom 67 were athletes and 56 controls. Since this was a questionnaire study and, hence, subject to response error, particularly with regard to cause of death, it was decided to determine the validity of the responses. Therefore, data from the death certificates were obtained in 104 cases. List B of the "Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death" [14] was used for the classification of the causes of death. Errors in the causes of death were classified as major, minor, and those of insufficient information. A major error was listed when the questionnaire response was not pathologically related to the cause of death on the death certificate. A minor error indicated that the response and the actual cause were related pathologically although classified differently in the international classification.

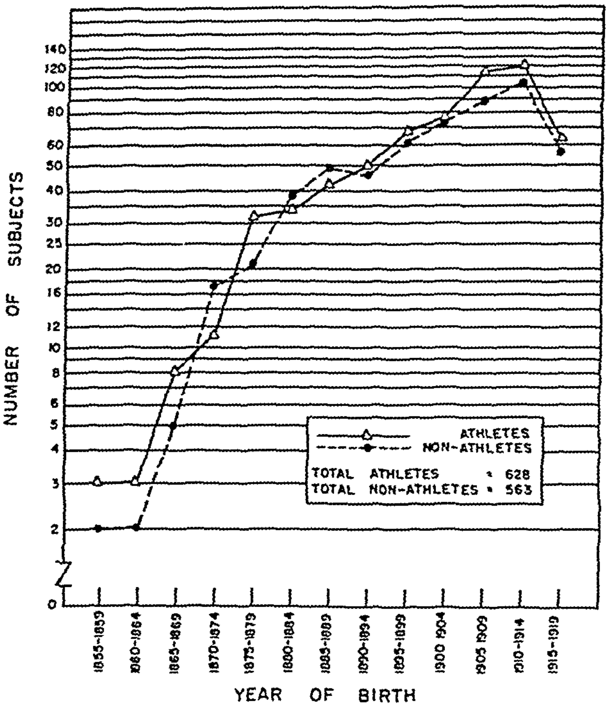

Fig 1 —Distribution of years of birth of athletes and nonathletes included in study

TABLE 1 —*Comparison of Athletes and Nonathletes, by Selected Characteristics*

Characteristic	Athletes, %	Nonathletes, %
Service in armed forces*	66.4	55.8
Branch of service*		
Army	70.1	82.7
Navy	23.2	13.9
Marine Corps	2.8	
Other	3.9	3.4
Activity in service		
Mild	13.7	18.9
Moderate	50.4	53.9
Vigorous	35.9	27.2
Married	96.9	97.0
Drinker*	77.6	66.5
Smoker*	68.7	60.2
Weight in college*	164 lb	153 lb
Weight gain since college	9.7 lb	10.4 lb

* These differences are statistically significant, i. e., it is unreasonable that chance would account for them

The validation results, in which the data from death certificates and the questionnaires were compared, were as follows: 1. In dates of birth, agreement was very good. Only 10 discrepancies were noted, with a mean error of 0.35 years, which was not statistically significant. 2. In ages at death, agreement was good. Twenty-two discrepancies were noted, with a mean error of 0.32 years, which also was not statistically significant. 3. Nineteen discrepancies were noted in causes of death. Two were major errors, 13 minor errors, and 4 were cases in which insufficient information was available to make a decision. Most of the errors noted concerned cardiovascular causes, particularly heart disease. While the layman is apparently oriented to the term heart disease, the death certificate might list the cause of death as coronary thrombosis or angina pectoris, which technically, for classification purposes, is erroneous. Because of this, fine classifications of causes of death from conditions of the cardiovascular area were not possible. Coarse classifications, however, were affected very little when questionnaire and death data were compared (fig 2).

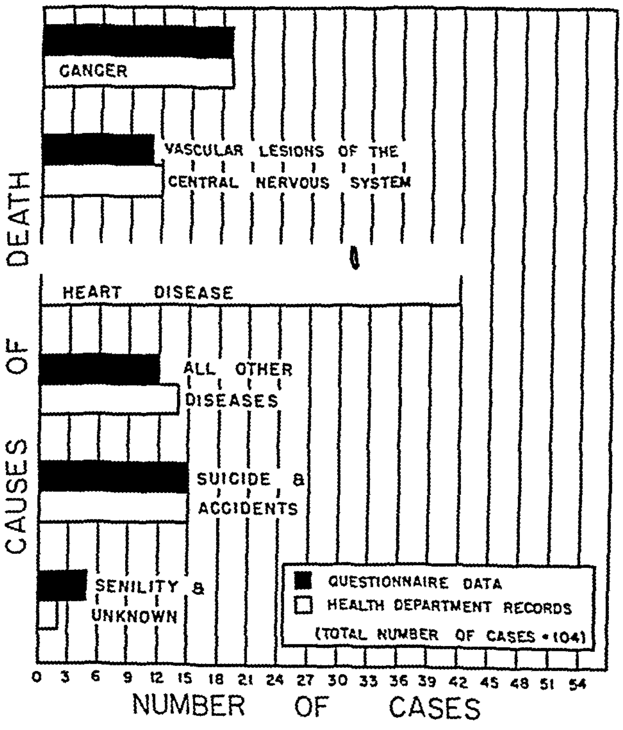

Fig 2 —Comparison of data on cause of death received from questionnaires used in study and of data from state health department records

The age at death of the athletes and nonathletes is compared in table 2. The difference in actual and expected age at death is not surprising, when we consider how highly select the men in attendance at college were during these years. Also, since the percentages of returns of the questionnaires in the two groups were 55.66 and 51.59, it is quite probable the sample became even more select due to the difficulty in obtaining data on those who died in the earlier years. What is of interest here, however, is that there is little difference existing between the two groups. This is in agreement with the studies by Dublin[12] and Rook.[13] Differences between the athletes and nonathletes in the distribution of causes of death, type of death (sudden or lingering), and causes of death of parents were statistically insignificant.

TABLE 2.—*Comparison of Age at Death of Athletes and Nonathletes*

	Mean Life Expectancy, Yr.*	Mean Age at Death, Yr.†	Difference, Yr.
All deaths included			
Athletes	65.96	73.86	7.90
Nonathletes	65.97	71.24	8.27
Excluding accidental deaths			
Athletes	65.96	74.43	8.47
Nonathletes	65.99	74.59	8.60

*Computed for the time when the athlete or nonathlete was in college, using the appropriate mortality tables.

†Actual ages of death were used where death had occurred. Otherwise this represents the individual's present age plus remaining years of life predicted from current mortality tables

Summary

The questionnaire method was employed in securing data on former college athletes (letter winners) and nonathlete controls. The results indicated that the longevity of athletes was approximately the same as that of controls and the distribution of causes of death was very similar. A significantly greater percentage of former athletes served in the armed forces and, of those serving, a significantly larger proportion served in the Navy and Marine Corps. A significantly greater percentage of former athletes smoked and drank, and their weight in college was appreciably greater. There were no significant differences in the number married, weight gain since college days, or strenuousness of activity while in the armed services.

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THE PHYSICIAN AS A SPORTSMAN

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• *The physician's interest in sports is twofold, for he may participate actively or he may be enlisted as an adviser on hygiene to athletic organizations or as a specialist in the treatment of athletic injuries. Several societies devoted to sports medicine exist, and important research is being done in this field. Physicians have also distinguished themselves as participants in many varieties of sport. It is necessary for the physician to adapt these activities to his changing capacities as he grows older. He may be inclined to exert himself immoderately after long periods of athletic inactivity and to view physical conditioning as a nuisance. His problem is to find time for frequent, regular, and moderate physical exercise and for relaxation and companionship. The many examples here given show that the problem can be solved.*

"It is very difficult for a physician in general practice to get a reasonable amount of exercise and play. He cannot take the time for golf, he dare not make a definite appointment with an opponent for tennis, and he must keep in communication with his office." Thus reasoned quite a few years ago a Dr. Weston, who was leading up to the fact that his favorite sport of archery could be readily practiced by a physician in spite of such inconveniences. In this present day of office hours by appointment, increased specialization, partnership and group practice, and a degree of prosperity that allows the physician to take time off when he feels like it, these difficulties may not seem to pose a serious problem.

Perhaps the thing that concerns the average physician today is not so much whether he can take time off for sports recreation but what sport he will find it best to pursue. The range of possibilities is wide and is limited chiefly by his preference and his pocketbook. Whether he believes in the therapeutic or the prophylactic values of exercise, he may be concerned as to whether he will overtax himself, particularly since his opportunities for recreational activity may increase as he advances in years. In this event, he might be more interested to hear from another sports fan, John DeVinne Singley of Pittsburgh, who has said, "It is essential that the heart muscle should not be overtaxed while exercising. Choose a type of exercise suitable to your years if you would derive benefit from it. As a physician, and from personal experience on the bowling green, I recommend lawn-bowling unreservedly."

Such evidence as is available indicates that, in the United States at the present time, there is no group of professional men that devotes more time to a greater variety of sporting and athletic activities than physicians. Although governing bodies of the various sports federations do not keep separate records of their membership according to occupation, the accumulated observations over a long period of time of interest in all sports, particularly with regard to record-breaking activities, coupled with a multitude of replies to a public appeal for information regarding the sports activities of physicians, have produced a sort of cross-sectional view of the extent of participation by our medical colleagues.

Professional Sports Medicine Groups

The great interest that many physicians have taken in the physiology of athletics is signalized by the organization and growth of such organizations as the International Federation for Sports Medicine (FIMS), the British Medical Sports Association, the American College of Sports Medicine, and the Western Council of Sports Medicine. The purpose of such organizations can best be summarized in the aims of the international federation: "To contribute toward the progress of medical sciences by the study of medico-athletic problems; to take all necessary steps for insuring that its conclusions are applied in all athletic and gymnastic activities."

The federation was established at St. Moritz, Switzerland, in 1928 and has since held congresses at Amsterdam, the Netherlands, in 1928; Turin, Italy, 1933; Chamonix, France, 1934; Berlin, Germany, 1936; Paris, France, 1937; Brussels, Belgium, 1939; Prague, Czechoslovakia, 1948; Montecatini, Italy, 1950; Paris, France, 1952; and Belgrade, Yugoslavia, 1954. It comprises a general assembly and an executive committee. Each national medical sports association appoints one delegate to the assembly. There are also guest members, one of whom is chosen for each country by the executive committee, and members of the executive committee, who are not national representatives. The executive committee, which is elected for a period of four years, meets every year. The congress of the general assembly is held every two years. It is supported partly by the host government and by members' subscriptions. There is a monthly official bulletin, *Studi di medicina e chirurgia dello sport*. National association members currently come from the following countries: Argentina, Austria, Belgium, Brazil, Czechoslovakia, Finland, France, Germany, Iran, Italy, Japan, Luxembourg, the Netherlands, Norway, Poland, Rumania, Spain, Sweden, Switzerland, the U. S. S. R., the United Kingdom, Venezuela, and Yugoslavia.

It may seem strange that our own sports-loving country is not represented in the federation by a national association, but there are some individual members from the United States. The closest thing we have to such an organization is the American College of Sports Medicine, which was founded April 23, 1954, for the following purposes: (1) to promote and advance scientific studies dealing with the effect of sports and other motor activities on the health of human beings at various stages of life; (2) to cooperate with other organizations concerned with various aspects of human fitness; (3) to sponsor meetings of physicians, educators, and other scientists whose work is relevant to sports medicine; (4) to make available postgraduate education in fields related to the objectives of the college; (5) to initiate, encourage, and correlate research; and (6) to publish a journal dealing with scientific aspects of activity and their relationship to human fitness.

Meetings of the college are held annually and alternately on the occasion of the annual meetings of the American Association for Health, Physical Education, and Recreation and of the American Medical Association. The third annual meeting was held in March, 1956, in Chicago. The membership is classified as fellows, associate fellows, members, affiliate members, and student members and is open to doctors of medicine, education, physical education, and public health, and to those holding master of science or arts degrees in fields related to physical education and biology. There are at present 78 fellows, 2 associates, 12 members, and one affiliate. A similar organization, the Western Council of Sports Medicine, was established in California in 1955. Although active membership is limited to physicians, laymen whose interest lies in this field are welcomed as associate members.

Participation in Sports

However, for every physician who carries his interest as far as joining such an organization, there are thousands who participate in sports either for exercise, recreation, relaxation, companionship, or simply because they enjoy competition. Some of the most enthusiastic sportsmen among the physicians are those well known to their colleagues because of their eminence in medicine and in other fields. Arthur Conan Doyle, who achieved fame as a writer, participated also in cricket, billiards, football, auto racing, sailing, rifle shooting, golf, and boxing. That remarkable American sage, Benjamin Franklin, who, although he did not hold a medical degree, was a member of several medical societies, including those of London and Paris, wrote many times on matters of public health and medicine and had a profound influence on medical thought in his day. He was an enthusiastic and accomplished swimmer.

There is probably no branch of sport that does not number among its participants physicians in the making, in medical school or postgraduate training, or in active practice. A surprising number have combined for a time the beginnings of a medical career with professional athletics. Naturally, those sports that depend on individual and unorganized participation draw the greatest numbers of physicians. The largest group of active participants are those who engage in hunting and fishing. The American Field Publishing Company states that there are more than 2,500 physician members of 300 registered organizations holding 600 or more pointer field trials in the United States every year. Regular or occasional fishermen among the profession are estimated to number between 40,000 and 50,000.

The taste of physicians as far as participation in sports is concerned seems to follow the national taste among adult males in comparative age groups. There is no one activity that seems to be particularly associated with the profession. The many physician golfers and proportionately fewer tennis players seem to follow the national average for participation in these sports, if allowance is made for the relative economic status of the two groups. The ability to belong to the local country club makes these sports more available for the physician, which compensates for the smaller amount of time he may be able to spend on them. Very few physicians apparently undertake sports or maintain their interest in them as part of a conscious program for maintaining or achieving physical fitness. Rather, they are inclined, when free to do so, to exert themselves immoderately after long periods of athletic inactivity. They also tend to ignore the importance of diet and abstinence (alcohol and tobacco) as preparation for athletic activity and to view physical conditioning by gymnastics as outmoded, impractical, and just a nuisance.

Outstanding Performers

In spite of this, the roll of champions and outstanding performers in all sports activities includes many who have achieved this eminence during their medical careers. The following list, with the sports enumerated in alphabetical order, indicates the names and accomplishments of those who have come to my attention. I make no pretensions of being all-inclusive and tender my apologies in advance to all those who are unknown to me or who have been overlooked or inadvertently omitted.

Archery.—Since archery as a sport has evolved from hunting, it is one of the oldest sports known. It made its appearance in the United States as an organized sport in 1828, when the Club of United Bowmen was founded in Philadelphia with Drs. Robert Eglesfield, Robert E. Griffith, and Samuel Griffith Jr. taking part. Since that time many physicians have participated in and achieved eminence in this sport. Henry B. Richardson of Boston was winner of the Grand National Title of Great Britain in 1908, J. W. Doughty of Washington won the American National Archery Title in 1913, and Erwin Pletcher was the National Field Archery Champion in 1949. Robert P. Elmer won many archery championships between 1911 and 1922 and has produced several authoritative books on the history and practice of archery. Other outstanding competitors have been O. L. Hertig of Pittsburgh, Saxton T. Pope of San Francisco, H. G. Goldberg of Philadelphia, B. L. Rawlins of Chicago, I. V. Cole of Seattle, H. T. Elliot of New York, and C. S. Case.

Auto Racing.—Since road racing in sports cars is essentially for the young man, one does not find too many physician racers. Probably the outstanding competitor at the present time is Sherwood Johnston of Greenwich, Conn. Among other victories he numbers the President's Cup Race at Hagerstown, Md., and the eighth annual sports car *grand prix* at Watkins Glen, N. Y., where he drove his D-Jaguar last year at an average of 81.92 miles per hour.

Baseball.—Participation in baseball after college days is practically limited to semiprofessional or professional leagues today. D. L. Adams and James R. Purdy were members of the old Knickerbocker Baseball Club in New York, one of the last strongholds of the amateur game. Medicine's outstanding competitor in professional baseball is Tommy Brown, who played third base for the New York Yankees to pay his way through medical school and internship.

Basketball.—The sport of basketball is also primarily professional after college competition and, because of the peculiar traveling requirements and long season, virtually excludes medical men. Al Van de Weghe of the New York Knickerbockers, however, helped to finance his medical education for several years while playing in the toughest professional competition.

Billiards.—While some may question the inclusion of billiards as a sport, it has always been reported as such. Apparently no physician has ever excelled as a professional, but the amateur three-cushion championship was held for three consecutive years by two medical men, A. J. Harris in 1925 and 1926 and L. P. Macklin in 1927.

Boxing.—It is a matter of interest that the only amateur ever to hold the world's heavyweight boxing crown was a physician. "Gentleman Jack" Jackson of England gained the world championship in 1795 and retired undefeated. He later opened a boxing school and taught Lord Byron, among others.

Court Tennis.—The most ancient and most intricate of all the racket and ball games, court tennis, still enjoys a limited patronage today in the United States as well as abroad. Many physicians in the eastern part of the United States have played this game of kings. Probably the most proficient were two from Boston, Channing Frothingham and G. S. Derby.

Fencing.—The sport of fencing has always attracted the interest of physicians. In the United States the names of B. F. O'Connor, Graeme M. Hammond, who founded the American League of Amateur Fencers, and Norman C. Armitage and John R. Huffman, who represented the United States in Olympic competition, stand out. Huffman accomplished a remarkable achievement for a non-European when he took sixth place in the saber event at the 1932 Olympics. Tibor Nyilas of Elmhurst, N. Y., has been seven times national saber champion.

Field Trials.—As previously indicated, the breeding, training, and hunting of dogs is a principal preoccupation of many members of the medical profession. A few of those outstanding in recent years have been Samuel Orr Black of Spartansburg, S. C., John H. Powers of Cooperstown, N. Y., past Grand National Grouse Hunting Champion, Frank H. Lahey of Boston, holder of the National Quail Championship in 1928 and 1934, Harold E. Langsdorf, Mount Holly, N. J., five times holder of the American Pheasant Championship and holder of the National Pointer

Championship in 1954, and Francis Record Whitehouse of Lynchburg, Va., winner of the National Beagle Club's annual field trial in 1955.

Fishing.—Since fishing is not for the most part a competitive sport among the fishermen, but rather a contest between man and fish, it is hard to pick out fishing "champions." Among the thousands of medical fishermen who have enjoyed this recreation in its many varieties may be mentioned two who were national champions in flycasting, E. A. McFarland and E. A. Fogle, and two whose record catches do not seem at first so remarkable but have stood for a long time in the record book of fishing. C. A. Abbott at Bordentown, N. J., in 1865 caught the largest yellow perch ever taken in fresh water, 4 lb. 3½ oz. W. J. Cook in 1916 in the Nipigon River in Ontario took the largest brook trout ever caught, which weighed 4 lb. 8 oz.

Football.—In the days when amateur football teams represented the university rather than simply the college, there were quite a few players who continued to be active while in medical school. The three-year rule today and the revival of professional football have limited the possibilities for physicians' participation. Nevertheless, two outstanding all-American players played the professional game to support their medical studies, both, strangely enough, for the Chicago Bears. Daniel J. Fortmann, now a surgeon in Hollywood, Calif., starred for at least five years after being all-American at Colgate University in 1935. William J. McColl, an all-American selection while playing for Stanford University in 1950-1951, has played for the Bears more recently. Medicine has made a unique contribution to football in the number of men who have undertaken college coaching. Clarence W. Spears, all-American at Dartmouth College in 1914-1915, coached for many years in the Big Ten. George W. Hauser, all-American at the University of Minnesota in 1916-1917, coached for many years afterward and is now a dermatologist in Minneapolis. The longest current coaching tenure of any physician coach is that of Edward N. Anderson, all-American at the University of Notre Dame in 1921 and now head football coach at Holy Cross. Marvin A. (Mal) Stevens was all-American at Yale University in 1923 and subsequently coached at the university, at New York University, and for the U. S. Naval Training Base at Sampson, N. Y. He is now an orthopedic surgeon in New York.

In the field of Rugby football, a remarkable record is held by Leonard Stokes of Guy's Hospital, Oxford, England, who drop-kicked an 80-yd. field goal while playing for England in an international match in the 1880's. A current star of Gaelic football is James Brosnan, now of New Rochelle, N. Y., who is a member of the County Kerry team that won the All-Ireland Championship in 1955 and that played in New York in 1956.

Golf.—Golf has the distinction among other sports of providing a semiofficial part of the program of the American Medical Association's Annual Meeting and of many other medical meetings. The American Medical Golfing Association held its 40th annual tournament June 11 in Chicago. All male members of the A. M. A. are invited to join this organization. Although thousands of physicians play golf every year, we have never produced as distinguished a champion as the dentists' Cary Middlecoff, now a professional. W. Tweddell, an Englishman, won the British Amateur Golfing Championship at Hoylake in 1927 and was one of the game's distinguished amateur players. Frank Deighton reached the quarterfinals of the same tournament this year. There are many eminent medical golfers who compete in the American National Senior Championships each year, among whom is former champion Ralph Nichols of New Haven, Conn.

Horsemanship.—Although many physicians ride for enjoyment and exercise, very few are active in equestrian competition. Benjamin Rush recommended riding very highly to his patients. John Yarbrough of Los Angeles is the head of the group who call themselves "Los Charros," who ride each year with Los Rancheros Visitadores.

Hunting.—Fox hunting has claimed the allegiance of many physicians in the United States as well as in the British Isles. Probably no one in this country has a more remarkable record of devotion to this sport than Misch Caspar of Louisville, Ky. He has been a winner of many trophies between 1906 and 1953 and during this time has owned over 2,000 foxhounds. Ira H. Rapp of Charlottesville, N. C., and Joseph F. Shuffield of Little Rock, Ark., are other notable exponents of this sport. Big game hunting and fishing attract many medical men. Some roam the entire world in pursuit of their hobby. Among the notable participants from the United States are Theo S. Stashak of Santa Rosa, Calif., Herbert J. Movius of Hollywood, Calif., and P. L. Riddell of Williamsport, Pa.

Lawn Bowling.—Lawn bowling is a rather old sport that maintains a steady popularity among a relatively small group of devotees. John DeVinne Singley of Pittsburgh, who was quoted earlier, is singles champion of his club. Raymond W. Sendker of Buffalo was Lakeside Doubles Champion in 1955 and has held several national championships.

Mountain Climbing.—The sport of mountain climbing claims the interest of physicians not only as a hobby but because it is considered essential today for all big expeditions to the Himalayas to have at least one physician climber as a member of the party. The British expedition that scaled Mount Everest in 1953 included three physicians, Michael Ward, chief medical officer, L. G. C. Pugh, medical physiologist, and R. C. Evans, who went with the final assault team. Stafford Matthews of Edinburgh, Scotland, a gynecologist, participated in the assault on Kanchenjunga and L. Bruce Meyer was on the 1954 climb of Makalu. Charles S. Houston of Exeter, N. H., was a member of the party that attempted to climb Nanda Devi in 1936 and led the unsuccessful attempt to scale Godwin Austen, or K^2, in 1953. Other noted American climbers are Benjamin G. Ferris and William F. Loomis, Boston, Roger S. Whitney, Colorado Springs, Colo., and Henry A. Buchtel, Denver.

Pistol Shooting.—J. R. Calkins of the United States was a member of the winning revolver and pistol team shooting at 50 and 100 yd. at the 1908 Olympic Games in London. Reginald Sayre of New York competed in many pistol-shooting events with notable success.

Polo.—Because of the restricted opportunities, elaborate equipment, and time required to play polo, few physicians have been known as polo players. A notable exception is Hugh B. Blackwell of New York, who represented the United States on one occasion in international competition.

Skin Diving.—Skin diving is one of the newest of all sports, but it already numbers many physicians among its followers. Two who have been interested in the medical problems involved are William T. Burns and Gordon Bateman of Long Beach, Calif.

Squash Rackets.—Squash rackets is the closed court game that has achieved the widest popularity in this country and throughout the British Empire. Notable physician players from the United States have been George M. Converse, Robert Dam, and William K. Miller of Philadelphia and Laurence M. Hutner, now of Los Angeles but city champion of Rochester, N. Y., from 1938 to 1942.

Squash Tennis.—Squash tennis has never been popular except in the northeastern United States. Alfred Stillman of Boston was the first national amateur champion and ruled in 1911, 1912, and 1914. H. R. Mixsell of New York was veterans' champion many times. In more recent years, Daniel C. Patterson of Bridgeport, Conn., and C. J. MacGrime of New York have been outstanding players.

Swimming.—Medicine has produced three Olympic swimming champions from the United States. G. E. Sheldon won the Olympic springboard diving championship in 1904. George Kojac, formerly of Rutgers University, in the 1928 Olympics won the gold medal in the 100-m. backstroke, was fourth in the 100-m. free style, and swam on the 800-m. relay team, which took first place. Major Sammy Lee, ophthalmologist in the U. S. Army Medical Corps, was Olympic diving champion from the high platform in 1948 and 1952 and climaxed his career in 1953 by becoming the only physician to win the James E. Sullivan Memorial trophy for being the outstanding amateur athlete of the year in the United States.

Table Tennis.—Table tennis has many physician players, but there are very few who enter competition. A successful competitor is Peter Fisher of Seattle, who formerly shared the Pennsylvania State Men's Doubles Championship and last year shared a similar title in Seattle.

Tennis.—The physician to be best known as a tennis star was probably James Dwight of Newport, N. Y., who five times, between 1882 and 1889, shared the national men's doubles championship. Undoubtedly the best tennis player–physician is David G. Freeman of Pasadena, Calif., who was once ranked no. 4 nationally in singles. Reginald Weir of New York has consistently ranked high in his district, as have Paul Newton of Oakland, Calif., and Peter Fisher of Seattle. J. A. Crane of Berkeley, Calif., was in 1955 ranked, with his son, Michael, no. 1 in father and son doubles by the United States Lawn Tennis Association.

Track and Field.—Some of the most outstanding athletic achievements of physicians of all time have been in track and field competition. Paul Martin of Switzerland won the silver medal in the 800-m. run at the 1924 Olympics while a medical student. Patrick O'Callahan of Roseville, Tipperary, Irish Free State, is the only physician to have won the gold medal twice in the Olympics, having been the champion in the hammer throw in 1928 and 1932. John E. Lovelock of New Zealand won the Olympic 1,500-m. run in 1936 and was also holder of the world's outdoor records for the mile as well as for 1,500 m. Arthur Wint of Jamaica, West Indies, won the gold medal in the 400-m. run in 1948 while a medical student. Roger Bannister, now of Guy's Hospital, Oxford, England, a keen student of the psychology and physiology of distance running, was the first man to run the mile in less than four minutes. Although he soon lost the world record to John Landy of Australia, he was able to beat Landy in near-record time in their famous race at the British Empire Games in Vancouver, British Columbia, Canada.

Although the United States has not produced any physicians who were world champions in track and field, we do have two noted competitors. Charles Robbins of Middletown, Conn., is the holder of 11 national titles in long-distance running events. He twice has been winner of the five-mile road race at Manchester, in which he competes annually. John Kingsley Lattimer, formerly of Columbia College and now professor of urology at Columbia University College of Physicians and Surgeons, held the Amateur Athletic Union 200-m. hurdles record for 12 years. He won the Millrose Games 50-yd. dash while a student at the latter college and later, while serving in the U. S. Army in Europe, he won the hurdles championship for the Seventh Army in the G. I. Olympics.

Yachting.—Sailing and powerboating rank high in the esteem of several thousand physicians in the United States. Britton Chance of Philadelphia became our only Olympic gold medal winner in this field when he sailed his 5.5-m. yacht to victory in 1952 at Helsinki, Finland. C. Darwin Jurss of Milwaukee won the Great Lakes sailing championship in 1936 and Benjamin Sawyer of Middletown, Ohio, won the Highlander National Class Championship in 1955. Some sort of transatlantic record was recently set by Hans Lindemann of Germany, who crossed this year alone from Liberia, Africa, to Haiti in 65 days in an overdecked canoe.

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Malignant Tumor Cells.—The structural pattern of a malignant tumor cell is sufficiently distinct from that of the normal cell to be readily identified in most instances even when viewed as an individual cell. The study of exfoliative cytology on which we depend for early recognition of cancer is based upon these observations. The changes most helpful for diagnosis of a tumor cell are nuclear, although cytoplasmic pattern, even in the light microscope, sometimes determines the type and source of the abnormal cell. The nuclear aberrations, the decreased cytoplasmic nuclear ratio, the coarser, more irregular chromatin pattern, the large, more numerous nucleoli, and heavier nuclear membrane are features in daily diagnostic use. No two tumors are alike and there is characteristically great cellular variegation in a single tumor, yet most tumors have certain morphologic features in common that are sufficient to enable us to say, "These look like cells of a malignant tumor."—E. E. Sproul, M.D., Particulate Components of the Cytoplasm, *Laboratory Investigation*, March-April, 1956.

RELATIONSHIP OF PHYSICAL FITNESS TO ATHLETIC PERFORMANCE AND SPORTS

Thomas K. Cureton, Ph.D., Urbana, Ill.

• *Physical fitness leads to better athletic performance, and persistent training will usually develop physical fitness. Detailed analyses of the anatomic and physiological characteristics of famous athletes show that it is possible to make fairly reliable predictions of athletic performance. Scores obtained by various static and dynamic tests exhibit various degrees of correlation with the scores made in competition, and it has been easy to pick out the tests that give the highest coefficients of correlation. Dynamic tests thus are shown to have higher predictive value than static tests. Type of physique, strength and power, respiratory efficiency, and cardiovascular components are among the factors that determine performance, but no two, or three, or four factors, even when combined in an optimum manner, measure all aspects of fitness. Fitness tests applied to former champions gave the best results in those athletes who were in continued training. Endurance training makes marked improvements in cardiovascular function. Ability of the endurance athlete to use oxygen is related to circulatory and respiratory capacity, but in sprints, weight lifting, and swimming there are many other important specifics.*

The relationship of physical fitness to sports is a two-way connection. Physical fitness surely leads to better athletic performances, and persistent repetition of daily training will usually develop physical fitness according to the character of the sport concentrated upon. The training for various sports differs, inasmuch as distance running is different from power performances, as in the high jump, shot-put, short sprint, or discus throw, and swimming 400 m. (as has been done by Boiteux, Hashizumi, and Konno) is different from pistol shooting, wrestling, or weight lifting. Success in such individual events depends upon the optimum combination of mental attitude, skill, and fitness. The great champion is apt to have these qualities and also the right body for the event. These characteristics should be illustrated to make them clear. Let us consider the types of fitness shown in two great athletes, Emil Zatopec and Roger Bannister.

Emil Zatopec has a lean, medium build (68.6 in. [174.2 cm.], 149.5 lb. [67.8 kg.]), with mesomorphic legs somewhat longer than usual and rather small (almost ectomorphic) chest and arms, and obviously carries an extremely small amount of dead weight. His legs are unusually strong. In his 5,000-m., 10,000-m., and marathon victories at Helsinki, Finland, in 1952, the peculiar nonuse of his arms, beautiful evenness of leg action and relaxed flatfoot style in his fairly short stride, and tantalizing head-turning and facial grimaces were interesting to watch, but in the last third of each race he left his competitors, with demonstrations of endurance that astounded everyone. The seven-year (1945-1952) laboratory record from Prague, Czechoslovakia, made available to me by Jiri Kral, shows his steady improvement in circulatory-respiratory capacity, which reached a climax at Helsinki. The scientific report states, "Zatopec improved and strengthened his natural somatic qualities with industrious training and with exercise until he reached his advantageous constitution of today . . . he went through and is constantly going through perfect many-sided physical training, which in the last analysis is the most important and deciding factor in the case of peak endurance sportsmen." It is remarkable that he did not even interrupt his training for military service. In the winter he ran in heavy boots in the forest or along some road. He trained both winter and summer. One minute after a 5,000-m. race in 1947, his blood pressure was 210/30 mm. Hg and his pulse rate 148 beats per minute. Before the race his blood pressure was 142/80 mm. Hg and pulse rate 68. In 1949, after his 10,000-m., world record run of 29 minutes, 21.2 seconds, his blood pressure one minute after the race was 160/40 mm. Hg and his pulse rate 150 beats per minute.

Kozik described Zatopec's "victory of the will" in 1949 and told of Zatopec's practicing breath-holding to train his will as he walked to work, counting poplar trees along the side of the road. He struggled with breath-holding day after day, "until he felt pressure in his head, weight on his chest, felt himself choking and felt like he was losing consciousness—then he fainted and dropped to the ground." Thus, Zatopec trained his will. Any runner who beat him had to beat such a will, not only a style of running or a body type. In 1951 and 1952 he trained by breathing oxygen mixtures and cultivated the relaxed upper-body style that enabled him to breathe the best. Such breathing of oxygen has been cited by A. V. Hill and Roger Bannister as being a possible means of conditioning the lung epithelium (through which oxygen and carbon dioxide must pass). In respiratory values, Zatopec had much higher than average values in volume of maximum ventilation, and, over four years of training, he increased the value for frequency of ventilation during exercise to three times that at rest. Seliger showed his pulse curve to be of the strong sympatheticotonic type. We have shown the same (fig. 1).

The results of tests made in 1951 by Hornof and Kremer in Prague showed an amazing ability of Zatopec's blood circulation to adapt to exertion. In the Harvard five-minute step test, the three pulse rate counts taken (after five minutes of stepping onto a 20-in. bench at the rate of 30 steps a minute) at from 1 to 1½, 2 to 2½, and 4 to 4½ minutes after the exercise period were 27, 29, and 31 beats, totaling 87 beats. In our records, only Bannister has recorded as good a test. In 1951, in the Flack test, Zatopec blew with a force of 40 mm. Hg for 60 seconds. After 30 step-ups in a minute, using a chair, he blew for 55 seconds. These figures are at the very top of our scales. In the report of Hornof and Kremer, the data on oxygen intake during the effort are missing, so we have only a partial fitness report.

Roger Bannister demonstrated some remarkable measurements of fitness when we tested him in London, England, in May and June, 1952, at the Royal Free Medical College. In the regular Harvard five-minute step test, his pulse rate was 108 beats per minute within the first 15-second interval after the effort, and there were 29 beats in the 1 to 1½-minute recovery interval, 29 beats in the 2 to 2½-minute interval, and 29 beats in the 3 to 3½-minute interval, totaling 87 beats. This equaled Zatopec's score. So far as we know, these are the two best records on this test. On another day Bannister performed remarkably in our "all-out step test," doing 40 steps per minute on a sturdy chair, 17 in. in height. At 5¼ minutes he was almost "all-out," as his legs began to tire obviously. We were using a large single Douglas bag to collect his exhaust gas. When this was full, we stopped him. Throughout the test he had the two-way valve in his mouth and his nose was clipped. In the first 15 seconds after this test, his heart rate was 120 beats per minute, which we consider remarkable. His systolic blood pressure after one minute was 170 mm. Hg, and his diastolic pressure was 60 (phase 4). The significant points are his extremely low pulse rate of 120 beats per minute and the drop of his diastolic pressure from 78 while lying (systolic was 114) to 60 mm. Hg (phase 4) while sitting (his pressure while standing was 124/86 mm. Hg).

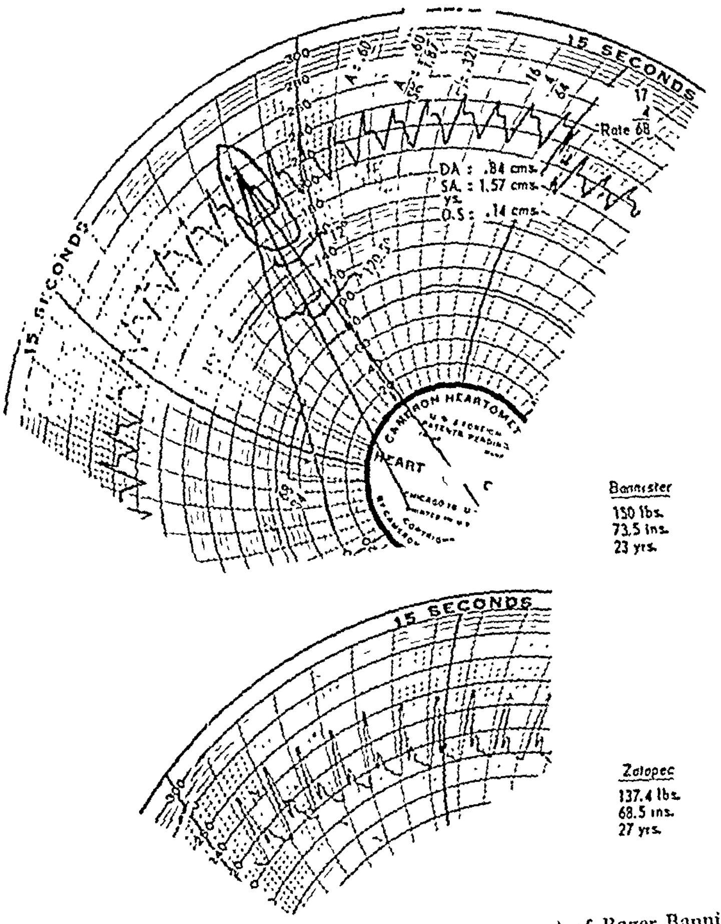

Fig. 1.—Basal sphygmograms (brachial pulse waves) of Roger Bannister and Emil Zatopec.

Bannister's heart in diastole is large and strong, like that of a racing greyhound (fig. 2). The transverse diameter was found to be 15.4 cm. and the frontal area 168.4 sq. cm. The internal chamber volume was calculated by the Keys and Friedell equation to be 1,068 cc., which, divided by body weight in kilograms, gave 15.65, the largest ratio found in our examination of several hundred normal subjects. The ratio of right to left diameters is 1:2.27, or just normal. Similarly to the Nylin ratio of volume to stroke volume (11.82), we used an inverted ratio: output in square centimeters (by brachial sphygmogram) to heart size in square centimeters (taken as the area of the heart in the diastolic phase on frontal x-ray). This index has a correlation of 0.68 with the gross oxygen intake (liters per kilogram of body weight) and with the time of the "all-out" treadmill run. Bannister had a result of 1.911, in spite of his large heart size.

Under conditions of hard work, Bannister's average oxygen intake was 3.226 liters per minute in our "one-bag oxygen-intake test," which is a high value for the 40-per-minute 17-in. chair-step test, with a respiratory quotient of 0.93. The distress that he built up during this effort was an oxygen debt of 0.0097 liters per minute per kilogram of body weight, or 3.473 liters of oxygen deficiency, which is very low. His pulse rate in the 15-second interval immediately after the test was, as stated, 120 beats per minute. In this all-out step test, his breathing was full and regular throughout. There were no signs of extreme distress, no extreme tensing, no facial grimaces, and no rapid

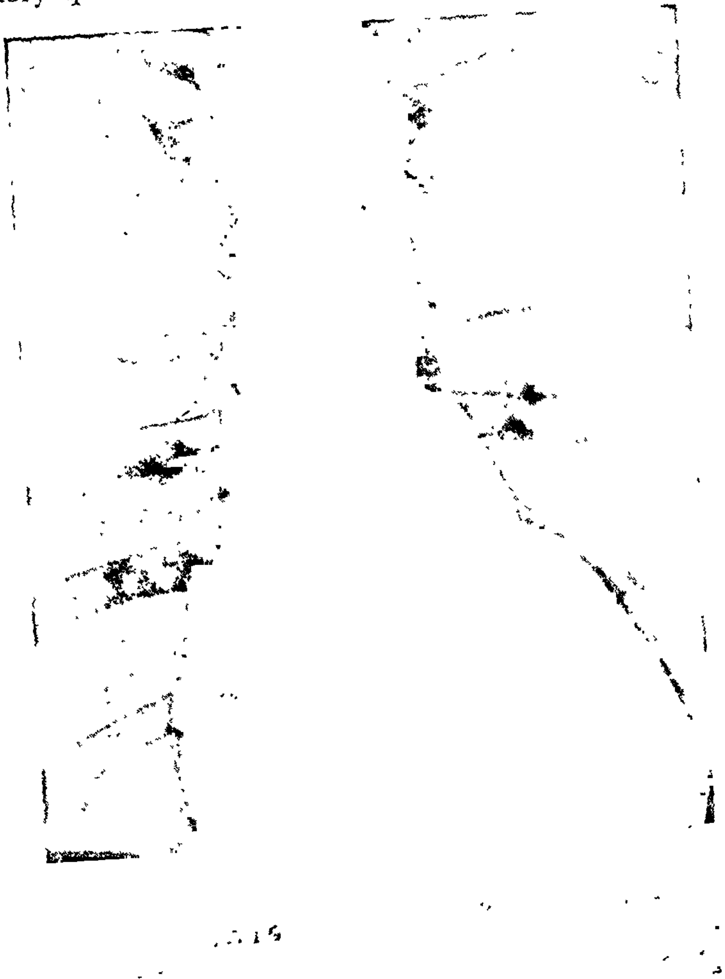

Fig. 2.—X-ray of Roger Bannister's heart in diastolic phase taken in May, 1952.

shallow breathing. The figures show that Bannister's oxygen deficit (debt) was very low. This was positive evidence of excellent adjustment to a very hard rate of work. The low pulse rate of 120 beats is a record among our observations, and his postexercise blood pressure of 170/60 mm. Hg was relatively low. It is significant that his diastolic blood pressure dropped during the work from 78 lying to 60 sitting and his standing from 86 to 60. We believe this drop in phase 4 of the diastolic pressure is related to cardiovascular adjustment to continuous and rapid work. Lack of adjustment is shown by a rise in diastolic pressure.

Bannister's best performance up to May, 1952, in the 1,500-m. run was 3 minutes, 48.4 seconds, and in the mile, 4 minutes, 7.8 seconds. In the July, 1952, Olympic Games at Helsinki, he ran the 1,500-m. run in 3 minutes, 47 seconds. He was remarkably good at stepping up and down on a chair at 30 or at 40 steps per minute. His gross oxygen intake per minute per kilogram of body weight of 0.0517 liters is the highest we have obtained of some 100 runners and athletes who have taken our 40 steps per minute all-out step test, in this he lasted 5¼ minutes. The highest precordial T wave in an electrocardiogram taken at rest was 25.3 mm. high, which was in keeping with his heart size of

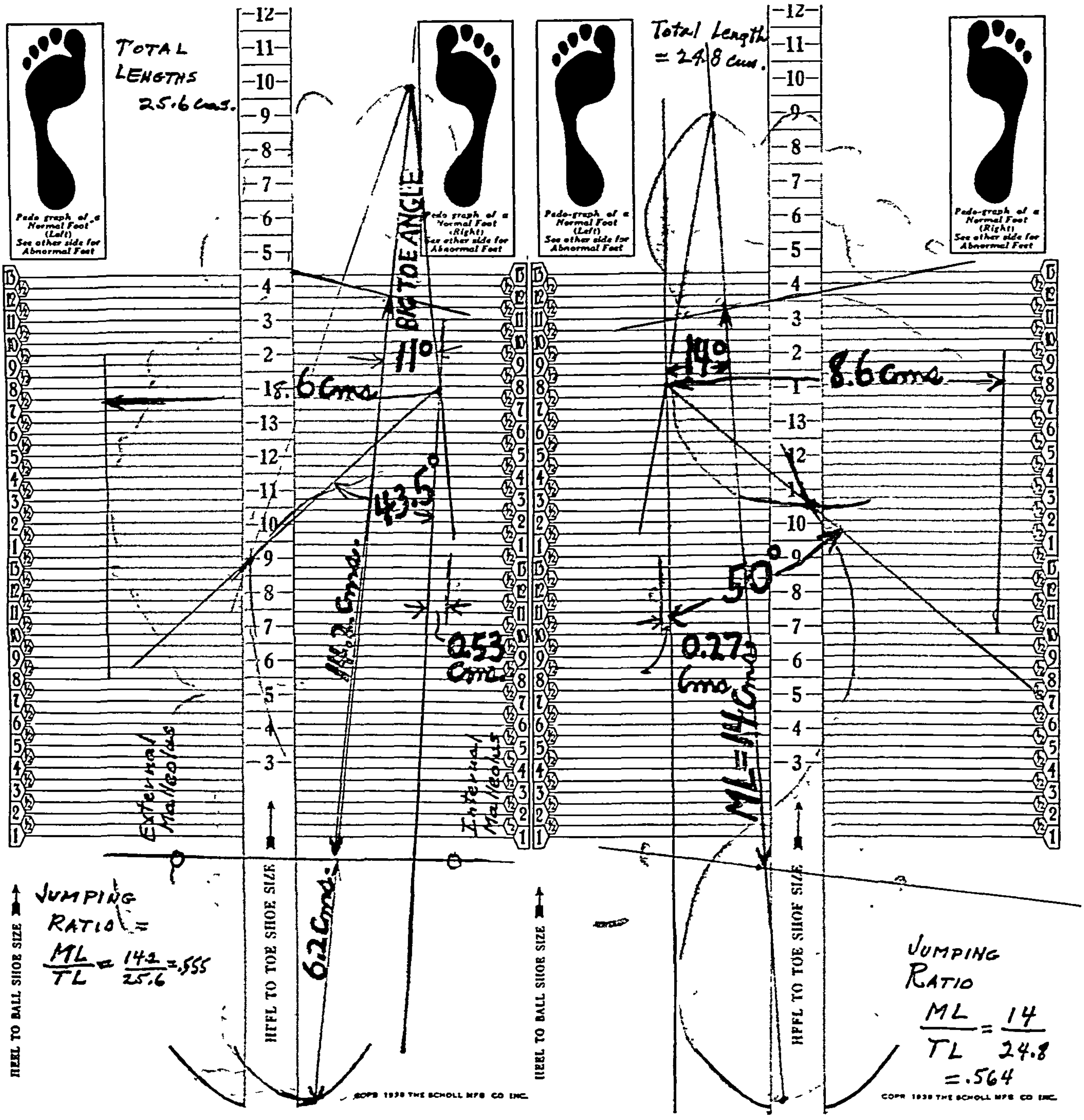
TOTAL LENGTHS 25.6 Cms.
Pedo-graph of a Normal Foot (Left) See other side for Abnormal Feet
Pedo-graph of a Normal Foot (Right) See other side for Abnormal Feet
BIG TOE ANGLE
11°
18.6 Cms.
43.5°
14.2 Cms.
0.53 Cms.
External Malleolus
Internal Malleolus
6.2 Cms.
JUMPING RATIO = ML/TL = 14.2/25.6 = .555
HEEL TO BALL SHOE SIZE
HEEL TO TOE SHOE SIZE
Total Length = 24.8 Cms.
14°
8.6 Cms.
50°
0.27 Cms.
ML = 14 Cms
JUMPING RATIO ML/TL = 14/24.8 = .564
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Fig 3 —Roger Bannister's footprints, showing comparative measurements

25.1% larger than normal according to the Ungerleider-Clark and Gubner tables. After his all-out step test his quickness of recovery was amazing, since he had a postexercise pulse rate of 108. Beyond any doubt, these wonderful circulatory measurements explain his ability to hold the pace of 57.5, 60.7, 62.3, and 58.9 seconds per lap in his mile run at Oxford on May 6, 1953, or of 59.2, 59.8, 59.6, 60.2 seconds at Vancouver, Canada, on Aug. 7, 1953.

In a lecture in London, on May 5, 1952, I predicted that Roger Bannister had the potential to run a mile under four minutes, but his legs needed further seasoning and his schedule of three workouts per week was inadequate. I recommended some leg-training exercises and in a long talk told him that I thought he could do it. The London *Daily Mirror* published my prediction. A year later, the day after Bannister did it, the prediction was republished by the same paper. In New York, on the day after the run, he said that his new record was partially due to taking up an improved and intensified training program. When we tested him we were amazed that he could do only 15 straddle-chins, 14 floor push-ups, 38 squat jumps, 75 side leg-raisings (right and left), and 35 sitting tucks and at his poor flexibility. He was a good jumper and excelled on the agility run. In the 18-item all-round motor test, he was poor, scoring only 7 out of 18, missing all three of the balance tests, two of the flexibil' ts, the breath-holding test, and all of the mus- durance tests. It was plain to me that Bannis- was a great running type, rangy and lean, with powerful lungs and a crural ratio of 1.423, as high as our tables record. His long legs and trunk length class him as the running type. His running coordinations and breathing were beautifully developed. His feet are of the springy, running-jumping type (fig. 3) with good arches, almost no pronation and a long forefoot (ratio of left foot, malleolus length/total length = 0.555; right foot, 0.564).

Bannister has certain important psychological characteristics worth mentioning. On Cattell's 16-factor personality test, he was extremely high in the E and Q-2 factors, indicating extreme dominance rather than submission and extreme independence of spirit. His very high amplitude precordial T wave (25.3 mm.) and high systolic amplitude of the brachial pulse wave (1.57 cm.) suggest that he is also high in factor F (animation versus despondency). In Cattell's test his percentile rank was 80. His basal metabolic rate was +21.4%, or 44.9 calories per hour per square meter of skin. His own interpretation to us was that it was a matter of will to run the mile in under four minutes, but one day, when he felt like giving his all, he would do it. In more technical aspects, Bannister demonstrates the great importance of training by breathing oxygen mixtures and practicing regulation of breathing.

Role of Athletic Training

The role of athletic training for physical fitness is further typified by the case of the great Japanese swimmer, Furahashi. In 1949, he set magnificent world records in the 400-m. swim (4 minutes, 32.6 seconds) and 1,500-m. swim (18 minutes, 19 seconds) at Los Angeles. He was in magnificent physical condition. He was then a college student and free in the summer to train hard for from three to six hours per day. Between that time and 1952, he had been graduated and had settled down to an eight-hour working day. When he did so poorly at Helsinki, being shut out of the 1,500-m. swim and finishing last (4 minutes, 42.1 seconds) in the finals, we asked him the reason for his decline. His simple answer was, "No time to train hard anymore." It is believed that athletic endurance is developed mainly by training day by day. Whereas Zatopec did not race hard until he was 19 years of age, Roger Bannister before he was 12 years of age began cross-country running and competition in track. From 1941 to 1952 he trained regularly in sports, including some rowing and Rugby football during 1944-1946. From 1946 on he specialized in track but did cross-country running during the winter to build endurance.

Predictions of All-Round Athletic Success

Several methods have been used to predict relative success in college athletics. DiGiovanna studied 18 measures in relationship to eight sports and concluded that the athletes in general were differentiated from normal young men by having more explosive power, by being larger and heavier, and by having greater arm and leg strength. Each sport was shown to have its own unique pattern of factors for success, but, in general, athletes are typically stronger and heavier and are more powerful (by strength multiplied by vertical jump) than nonathletes of the same height. While DiGiovanna's study in 1943 showed statistical significance for most of the various measurements, no composite formula was developed beyond the use of MacCurdy's power formula of strength multiplied by velocity, simulating the physics equation of power = force × velocity, developed in 1933. This was based upon the combination of two lines of research previously published by Rogers in 1925 and Bovard and Cozens in 1928. In 1887 Dudley A. Sargent had published significant articles on "The Physical Characteristics of the Athlete" and, in 1921, "The Physical Test of a Man." Sargent's work was empirical rather than based upon modern statistics of prediction, but his insight was remarkable. He was a leading advocate of the pulley-weight exercises and of dynamometer strength tests. Several workers have shown the basic importance of strength to athletic performance. Several others have emphasized speed.

The next important advance came in 1940 with the work of Leonard A. Larson, who made a careful statistical analysis of the data of 15 motor tests selected on the basis of their presumed relationship to all-round athletic ability. Larson demonstrated that "dynamic" events, in which a man lifted, pushed, pulled, or propelled his total body weight against gravity, had much more relative validity than the older static tests of dynamometric strength, which in themselves were more valid than any combination of body measurements or proportions. Larson produced a simplified weighted formula: predicted athletic capacity = 2.12 (no. of chins) + 2.27 (vertical jump) + 1 (no. of dips on parallel bars) (in standard scores). Larson further adjusted his prediction tests in 1941 to add the dodge run (outdoors). He also continued to study various combinations and recommended simplified tests to the U. S. Army Air Force composed of (1) baseball throw for distance, pull-ups, and vertical jump and (2) 300-yd. shuttle run, pull-ups, and sit-ups. In using these tests with 1,031 college freshmen, Landis showed that a course in basic conditioning produced the greatest improvements in a semester of training, with tumbling-gymnastics next, compared to swimming, tennis, boxing, weight-training, volleyball, and wrestling.

In an analysis of the Larson-type tests, we found certain omissions that made us dissatisfied with the tests. One of these was the omission of any item that took longer than two minutes to perform. A comprehensive monograph entitled "Endurance of Young Men," published in 1945, sustained our position that the mile run had greatest all-round predictive value in a 28-item athletic criterion. Next came chinning the bar, floor push-ups, hops, dips on parallel bars, forearm push-ups, sitting tucks, and side leg-raisings. Some items rated surprisingly low, including the elbow-to-knee sit-ups, the step test, the stick body, leg lifts, sit-ups (feet free), chest-raisings and V-sit test. Our factor analysis and test construction work yielded several test batteries, which have been published. The University of Illinois has since used the three-item all-round muscular endurance test (0.366 chinning the bar + 0.401 sitting tuck + 0.411 mile run). Our laboratory has used the four-item indoor test (0.323 chinning + 0.279 floor push-up + 0.282 sitting tuck + 0.365 hop). In these equations standard-score results are multiplied by the weightings, the results added, and the totals rated by our published tables. Track sprinting aptitude is shown by the total-body-reaction-time test published in 1951 by Garrett and me. It is fairly highly correlated with the vertical jump and the Illinois agility run test. High-jumping ability is fairly predictable from the vertical jump test, with height and length of legs related to length of trunk.

I made a comprehensive study of the relationship of various physical fitness tests to the total of a 22-item criterion in 1947. The highest (most valid) type test was the 18-item stunt type test or the 14-item motor test; next was strength (sum of two grips, back-lift, and leg-lift on dynamometers); next was somatotype rating; and next the Harvard five-minute step test. The 18-item motor test has been widely publicized. In addition to those mentioned, a few other desirable but less valid tests are the Schneider index, vital capacity, adipose tissue, and a body-type picture with posture measurements. The 14-item test revealed an appalling amount of unfitness among the young men coming to college from the high schools. The 18-item test has shown even greater proportions of unfitness among the adult population, both men and women. An interesting observation is the fact that a great runner like Roger Bannister could be so poor in sections of this test involving balance, flexibility, strength, breath-holding, and even aspects of muscular endurance. No single sport develops all the types of fitness sampled even by this test. The case for all-round fitness has been presented by a competent committee at Springfield College, Springfield, Mass., and also by a competent committee composed of the entire staff at the University of Illinois.

Superior short-duration athletic performance involves power as stated. Several studies have separated power into strength and velocity (speed) components. The first notable study of this type was by Charles H. McCloy of Iowa University, in 1932. Other studies have followed by Rarick, in 1937; Hutto, in 1938; Coleman, in 1940; and Carpenter, in 1941. McCloy in 1940 in *Psychometrika* summed up this particular line of research, particularly with respect to the use of the factor analysis method.

Body Build and Athletic Performance

A broad view of physical fitness includes the structural aptitude (body build) for the particular event. Being "fit for the event" involves, first of all, a physique appropriate to the event. Thus, the high jumper is usually tall and slender, relatively long in the forelegs to thighs area, and with a long metatarsal arch compared to the length of the whole foot; he is built somewhat like a grasshopper, with long forelegs and feet along with strong thighs and light body (as are DeSilva, 1952 hop, step, and jump Olympic champion, and Jesse Owens, 1936 Olympic sprint and broad-jump champion). The typical diver is medial and muscular in build (as are Clotworthy, Browning, and Harlan). The middle-distance runner is generally long-legged, with a relatively lighter upper body (as are Sowell, Wint, Bannister, Landy, and Tabori). The typical soccer or football athlete is muscular and may be tall, medium, or short. The weight lifter is usually seen as a heavy (muscular and fat) type with unusually short levers (as are Anderson, Davis, and Kono).

Endomorphic persons are notably absent in any distribution of athletes. These are types with long and bulky viscera, large amounts of fat and fewer muscle fibers than are needed for athletic success. Some mesomorphic wrestlers grow fat, but they are not truely endomorphic. Kohlrausch, Arnold, Telkka, Bartolome, Sills, and I have made various studies of athletes, utilizing anthropometric techniques. Sills and I have made adaptations of Sheldon's somatotyping method, which has also worked out well in the classification of aviators. There is extensive literature on the relationship of body build to athletic performance, which is summarized by the authors mentioned. An appropriate body type helps to win, but there are important exceptions to the rule, due to many years of developing skill, experienced judgment, and the will to win. There are some short tennis players, swimmers, and ball players as exceptions, just as there are some heavy golfers, pistol shooters, and sprinters, or short pole vaulters and basketball players, but we consider these to be the exception rather than the rule.

In making a prolonged study of Bob Richards, we found that he could run as fast with the pole as anyone and could spring exceptionally well onto the pole at the moment of take off, but his timing and speed of draw up were poor. Dick Ganslen coached him carefully on this point, and I advised a weight-training program for his hands, shoulders, and thigh taken one minute after this was 6.82; the 100-yd. drop-off (without a dive and all-out all the way) swimming endurance index was 1.5 seconds, and his ratio of heart output to heart size was at the top of the scale. We predicted his 100-yd. drop-off swim to be 55.6 seconds, and he swam 54.9 seconds with a 1.9-second drop-off. This test combines short-sprint speed for 60 ft. with endurance by the formula published by me in 1935: time for 100 yd. in seconds = 5.98 (time of 60 ft. sprint in seconds) + 2.88 (drop-off index) -2.63.

Other equations for the diagnostic analysis of swimming were published by Wilson and me, for predicting the short 60-ft. sprint (crawl and back and breast strokes). I also published the prediction equations combining the most valid factors for predicting success in 100-yd. and 440-yd. swims. This type of work significantly differentiates power and skill from endurance. Swimming for speed is shown to be mainly power and skill for 60 to 75 ft., but as the distance lengthens the circulatory-respiratory fitness looms as the dominating factor. Ford Konno and Yoshinobu Oyakawa, the great Hawaiian Olympic champions, have very flexible ankles, strong arms, and wonderful kicks, but their ability to hold such a fast pace over the longer distances is mainly due to relatively great circulatory-respiratory fitness and to their training diligently to hold the fast pace over a longer and longer distance. From our comparative studies of the Japanese and American swimming teams of 1932 and 1936, we demonstrated that the percentage of superiority of these Olympic men was mainly in circulatory-respiratory fitness, compared to groups of Yale University, Dartmouth College, and Springfield College groups. These data were published in 1932 and 1947.

The gross-oxygen-intake test is the most valid test of the ability of the heart, lungs, and muscles to circulate the blood. It has been applied most successfully to treadmill upgrade running, ordinary flat running, rowing, running in place, and swimming, but it has not as yet been related to other types of performances. It would be valuable to know the gross oxygen intake results on a variety of hard exercises. From available data in hand now, it seems clear that the test is most valuable as a predictor of performance in events of endurance that use a great deal of musculature and are continued to the point of virtual exhaustion.

Specificity of Physical Fitness Tests

The fact that fitness has many specifics, like a mosaic, has been hard to comprehend. It is clear that no single item measures all aspects of fitness. The truth is that no two, three, or four items, even when combined in an optimum manner, measure all aspects of fitness. The proof of this is reflected in the following research: 1. The Larson chinning–vertical jump–bar dipping test was correlated with my 30-item motor fitness criterion. The result was a correlation of +0.447 in 171 cases of young men in the service classes at the University of Illinois. The Larson weighted index correlated +0.338 with endurance, +0.383 with power, +0.492 with agility, +0.218 with dynamometer strength, +0.031 with flexibility, and +0.019 with balance. No prediction of body-type or circulatory-respiratory fitness from this Larson test was possible. 2. Any table of intercorrelations for measures of balance, flexibility, agility, strength, power, and endurance was shown to have a predominance of low correlations between the items. From the 30-item motor fitness criterion Welser, Huffman, and I made a simplified 7-item motor fitness test that included items of greatest all-round predictive value ($R=0.78$). The items included were dive and roll, medicine ball put, bar vault, chinning, leg-lifts and sit-ups, breath-holding, and man lift. 3. A factor analysis of 22 items of fitness gave six basic components: constitutional body type, thinness of adipose tissue, metabolic rate, pulse rate condition, strength, and coordination in gymnastic and tumbling stunts (14 or 18-item motor tests).

Cardiovascular Components

From available evidence there seem to be at least five types of cardiovascular condition, each of which may be called a component. First, the autonomic nervous balance (component 1) is determined by blood pressure, pulse rate, and pulse wave tests in the quiet state, from palmar skin resistance or conductivity, or by noting the rise in pulse rate after injection of atropine (vagus tone). Second, splanchnic tone (component 2) is the distribution of blood against gravity as noted in the change in pulse wave, pulse pressure, or pulse rate in changing from lying to standing or from sitting to standing positions. After a subject stands for a minute, any tendency of the blood to settle into the feet, legs, or splanchnic region will result in a smaller pulse wave, reduced pulse pressure, or a rise in pulse rate.

Third, efficiency in long submaximal work (component 3) is the ability to work economically at a submaximal pace for a long time as indicated by pulse rate, blood pressure, pulse waves, and oxygen-intake tests. A rise in pulse rate, blood pressure, and oxygen consumption indicates reduced efficiency, as does also a reduced pulse wave. Fourth, efficiency in athletic (racing) endurance (component 4) is the ability to work relatively long at a pace that will develop an oxygen debt of 3 or more liters (maximal exercise) or to work a long time at a set pace on the treadmill or in the step test. The higher the oxygen consumption, the better. An oxygen debt above 3 liters is proof of entering a semiexhausted state but is not reliable.

Fifth, recuperation after exercise (component 5) is the recuperation of pulse rate after relatively hard exercise as in the five-minute step test. Various tests have emphasized measuring the postexercise pulse rate, blood pressure and blood lactate levels, pulse waves, and blood pH concentrations. Exercise of a severe type produces changes in these, but, so far, evidence that the all-out performances can be predicted from such data is unsatisfactory. Lucien Brouha assumed that this was so, but in a series of studies I demonstrated very low correlations as reported in a 1945 National Research Council study on "Endurance of Young Men." Craig Taylor had even earlier, in 1943, severely criticized use of the blood lactate test in a report to the National Research Council. The lack of validity of this test was explained in work by

Sacks and Sacks and Shaw, in which they pointed out that in human subjects the amount of blood lactate from venous samples taken after exercise does not indicate the total amount of lactate in the body. Some lactate spills over into the urine.

I summarized these objections to the blood lactate test in 1951 in "Physical Fitness of Champion Athletes." In addition, Montoye used the data from the Harvard fatigue laboratory in 1953 to restudy the relationship of the "recovery index" and blood lactate level (taken five minutes after exercise) and showed a correlation between them of −0.470, between lactate level and maximum pulse rate of +0.131, and between recovery index and maximum pulse rate of −0.637. After 12 weeks of training, the coefficients were −0.722, −0.782, and +0.665 respectively.

Montoye found the Harvard (Brouha) step test to be of limited value, because correlations with a wide variety of strenuous work criteria are in general very low. They were half-mile run time, −0.232; ergocycle time, 0.091; maximum number of sit-ups, 0.286; cross-country running speed, 0.38; mile run without training, 0.31, and after training, 0.54; 300-yard run time, −0.272; treadmill run time, 0.4; order of finish in the Boston Athletic Association cross-country 'marathon, 0.32. It is agreed by several workers that the pulse rate after exercise is sensitive to training. Training results in a lowered maximum pulse rate and lowered blood lactate levels during a standard exercise, but Taylor's correlations of these with all-out run time are too low (−0.56 and −0.44 respectively) to be of much value in predicting individual performance.

Athletic training affects all of these components, but very specifically. We found that in six weeks of training a young male subject improved at 7 miles per hour but not at 10 miles per hour, when he ran three miles per day at 6 to 7 miles per hour. Many top athletes in component 4 have been shown to be ordinary or poor in certain of the other components. It has been reported several times that all-out running times could not be predicted from components 1, 2, 3, or 4. Great confusion can be eliminated by calling these cardiovascular components what they are and using tests of component 4 to predict athletic endurance.

Skill, Coordination, and Fitness

As greater and greater skill develops as a result of continual practice, the experienced athlete is able to accomplish a given stunt or race with relatively less effort. It was surprising to find that experienced athletes do not develop any higher oxygen debt (internal oxygen deficit) than nonathletes. My 1948 study shows that 18 normal (untrained) young men averaged 7.37 liters of net oxygen debt compared to 7.23 liters for 20 experienced varsity athletes. However, the athletes had greater gross oxygen intake (6.89 liters) compared to the nonathletes (4.06 liters), an advantage of 22 in standard scores, or an advantage of 71.2%. The athletes develop the oxygen deficiency at a faster rate (0.062 liters per minute per kilogram of body weight) compared to the nonathletes (0.047 liters per minute per kilogram of body weight). Most of all, the athlete has a greater aerobic capacity and does no more of his work on anaerobic capacity than the untrained man. This explodes the value of the oxygen-debt test as a test from which endurance performance can be predicted.

When A. V. Hill figured the oxygen requirement as net oxygen intake plus net oxygen debt divided by time of effort, he was interested mainly in accounting for the oxygen cost attributed to the exercise, and, from this point of view, he is absolutely correct. From the point of view of which test is best to predict the time of the endurance effort, the gross oxygen intake (liters per kilogram of body weight) gives a validity correlation of +0.87 compared to +0.57 for Hill's oxygen requirement, while the correlation of net oxygen debt (in liters) is +0.19, practically worthless. Why then should this part be used at all? If we use the rate of oxygen debt, we introduce the time of the effort in the denominator, which, of course, correlates negatively with the time of the run as the criterion, and thus the correlation is −0.60 but is spurious.

The trained athlete is usually more skillful and, hence, more economical. He breathes better, saves himself whenever possible, and avoids tenseness in any muscle group that would hinder circulation. With experience he learns to relax as much as possible. He uses muscle effort exactly where it is needed and then relaxes to let the blood flow and deep breathing to occur. Frequently, such skill is merely attributed to experience. To observe Herb McKenley finish a 400-m. run—or Rhoden or Kelly—is to witness such controlled relaxation in action. In the Helsinki games, Dick Cleveland was apprehensive and he tightened up, ruining his chances in the 100-m. swim sprint; whereas, Clark Scholes, a cooler and more experienced swimmer, relaxed a bit more and had better circulation with which to win. Cleveland made his world's record before a small crowd and against less formidable competition in his homeland.

It is not the purpose of this paper to cover mechanics of athletic performance, but scientific analysis of many events has yielded formulas for analyzing events such as a swim, sprint run, shot put, discus throw, javelin throw, pole vault, high jump, and broad jump. The physical economy is represented in such formulas. Performances follow, first of all, physical laws; then physiological adaptations and psychological adjustments further modify the effort. No physical performance is a simple matter. Reference to studies in mechanical analysis can be found in Webster's "The Science of Athletics," Bunn's "The Scientific Principles of Coaching," or in the research methods book of the American Association for Health, Physical Education, and Recreation.

The usual scheme of analysis is (1) to analyze the mechanics of the event; (2) to analyze the physical body build and aptitude of the performer; (3) to analyze the physiological fitness of the performer; (4) to analyze the psychological attitudes of the performer; (5) to get some physician to help remedy all health hazards, chronic ailments, or infections; (6) to prescribe developmental and conditioning activities for detectable weaknesses; (7) to plan a program of training to bring the performer to a peak at the needed moment; (8) to check the dietary regimen carefully and suggest possible improvements; (9) to seek ways of observing and studying the most competent performers; and (10) to arrange a progressive schedule of competitions to season the competitor, realizing that this takes time.

Age, Performance, and Fitness

The evidence presented by Ernst Jokl indicates that lifelong physical training exerts a powerful influence on inhibition of the usual decline in physical ability, athletic efficiency, and health, but evidence that the immunologic resources of the body are affected is not available as yet, nor is it claimed with respect to the more virulent infectious diseases. Jokl's data on 1,609 men, aged 40 to 84 years, and 98 women, aged 32 to 52, was taken in 1952 at the National Gymnastic Festival for the Old in Marburg, Germany. The absence of degenerative diseases of the cardiovascular system, of neoplastic growths, and of kidney ailments among the older participants lead Jokl to the conclusion that the lifelong practice of gymnastics and other athletic sports had maintained their health and fitness in a remarkable way.

Over the past 50 years, in Europe and in the United States, there has been a general lengthening of the period of optimal usefulness of men and women. Today the trend is for people to mature younger—estimates indicate that the menarche in girls occurs five years earlier than in 1875—and they live longer. It is believed that this trend is accentuated by sports and regular physical training.

Diem studied the performance in the last three Olympiads to show that more and more the participants are both younger and older, with many in their teens and many over 40 years of age. Among the medal winners at the 1932 Olympic Games in Los Angeles were two 14-year-old Japanese schoolboys in the 1,500-m. swimming race, Kusso Kitamura and Shozo Makino, of Japan, who finished a length ahead of every other contestant. Among the medal winners at the 1948 games in London were the 16-year-old Japanese discus thrower, Ko Nakamura, the 18-year-old gymnast, Anita Barwirth, and the 17-year-old decathlon champion, Bob Mathias. While Jokl and Diem cite many others, old and young, in a similar relationship, our own data show that the former Olympic decathlon champion and world's high jump record-holder in 1924, Harold Osborn, at 51 years of age, has taken extraordinary physical fitness tests as shown by our laboratory tests in 1951 and 1952. In Finland, in 1952, it was impressive to see Paavo Nurmi still running well at 50 years of age and Hannes Kohlemainen run up the steps of the campanile (tower) at the stadium at 68 with an amazing demonstration of fitness. We found René Cochet, the great tennis star, fit and playing in the national tournaments at age 50. Jokl has estimated this advantage in tennis, as preventive of physiological aging, to be 6 to 10 years.

In our data on the all-out step test at 36 to 40 steps per minute, there is a surprisingly poor relationship of age to stepping time or to gross oxygen intake among 55 former athletic champions ($r = -0.566$). There is a slight trend for the younger subjects to develop a somewhat higher oxygen debt ($r = -0.364$). The total net oxygen cost was positively related to performance time ($r = +0.547$), but the rate of net intake oxygen was poorly related ($r = -0.341$ for liters per minute and -0.179 for liters per minute per kilogram of body weight). Several older men, who had maintained regular endurance training, still had relatively high gross-oxygen-intake capacity and were able to prevent any rise in the diastolic (phase 4) blood pressure. A few could still produce a drop, characteristic of a youthful competitor with a cardiovascular system still capable of making a good adjustment to hard endurance work. For instance, Harold Whitlock, many times walking champion, at 48½ years of age, with a starting blood pressure of 140/80 mm. Hg had 186/74 after stepping all-out for 2.17 minutes at 40 steps per minute on the 17-in. bench.

In the past few years we have accumulated evidence that favorable adjustment of the cardiovascular system, usually with marked reduction of peripheral resistance, accompanies systematic and progressive physical training of the endurance type. An example of this is shown in the table. We are led to believe that either physical training has been misunderstood or it has never been understood regarding this type of beneficial effect upon the cardiovascular system. By the use of Kellogg's tables of blood pressure related to expected loss of life, we have consistently shown the reduction of systolic and diastolic blood pressures, the increased stroke volume, larger pulse waves, and improved endurance in all-out treadmill running that *accompany such training of six months to a year.*

Change in Peripheral Resistance Associated with Physical Conditioning

An illustration is given of changing peripheral resistance in a 47-year-old subject as a result of five months of physical conditioning in 1953. The method used is simply that of substituting the pretraining figures of mean blood pressure (P_m), stroke volume (V_s), rate of heart beat (R) per second and solving for total peripheral resistance (TPR).

Pretraining:

$$\mathrm{TRP} = \frac{P_m}{V_s \times R} = \frac{155}{29 \times 0.800} = 6.69 \text{ mm. Hg per cubic centimeter per second}$$

$$P_m = \frac{180+130}{2} = 155 \text{ mm. Hg} \qquad V_s = 29 \text{ cc./stroke} \qquad R = 48/60 = 0.800 \text{ second}$$

Post-training:

$$\mathrm{TPR} = \frac{P_m}{V_s \times R} = \frac{128}{75 \times 0.867} = 1.97 \text{ mm. Hg per cubic centimeter per second}$$

$$P_m = \frac{158+98}{2} = 128 \text{ mm. Hg} \qquad V_s = 75 \text{ cc./stroke} \qquad R = 52/60 = 0.867$$

Ratio of pretraining to post-training total peripheral resistance, $6.69/1.97 = 3.40$ or 3.40 to 1.

(This equation is essentially that given by Wiggers in his book "Cardiac Dynamics." Henry has also made use of the same type of equation in a recent article and accredits the earlier work of Wezler and Böger.)

The subject was given five months of conditioning work, which consisted of a 30-minute period of conditioning exercises on the deck of a swimming pool, followed by a shower and a 20 to 25 minute swim in a regular swimming pool, 76-78 F in temperature. The exercises were led by an instructor five days per week. Once each week the exercises were of the "test-exercise" type in which each exercise was done for as long as the subject could maintain it by voluntary effort.

By another calculation the volume elasticity was reduced from 3.45 to 1.60, a reduction of 53.6%. (The volume elasticity [E] equation is $P_s = V_s\ [TPR \times R + E/4]$ wherein, P_s=systolic pressure in mm. Hg and all other notation is the same as in previous equation.) Thus, we might say that the suppleness (give) of the large blood vessels above the heart was increased. It is not fully known how much of the effect is due to dilatation of the arterioles and possibly the capillary beds, but it would seem theoretically that both aspects had occurred.

*Changes in Peripheral Resistance Associated with Physical Conditioning**

Subject	Test	Av Pulse Rate, Beats/Min	Av. Systolic Blood Pressure, Mm Hg (182 118)	Av Diastolic Blood Pressure, Mm Hg	Av Blood Pressure, Mm Hg	Cardiac Output† Liters/Min	Converted Cardiac Output‡ Liter/Min.	V_s Cc./Beat.	R Beats/Sec	$P_m/V_s \cdot R$	TPR	Duration of Training in Conditioning Exercises
1	T_1	52	150	118	150	6.47	7.91	152	0.87	150/132.2	1.135(6)	T_1 to T_2=5 mo
	T_2	52	(144 106)	106	135	6.30	7.72	148	0.87	125/128.7	0.971(6)	(14.1% reduction)
2	T_1	60	124	74	99	4.68	4.93	95.8	1.00	94/98.8	0.985(3)	T_1 to T_2=5 mo
	T_2	58	100	74	87	6.06	6.81	117.0	0.97	87/113.4	0.767(4)	(23.2% reduction)
3	T_1	72	126	70	98	5.56	6.90	95.8	1.20	98/114.9	0.853(4)	T_1 to T_2=5 mo
	T_2	72	102	76	89	6.10	7.50	104.0	1.20	89/124.8	0.713(6)	(16.4% reduction)
				Control (Changes over 2 Mo.)								
4	T_1	60	100	75	88	5.48	6.82	113.7	1.00	88/113.7	0.774(5)	T_1 to T_2=2 mo
	T_2	64	105	69	87	5.03	6.32	98.8	1.07	87/105.7	0.823(2)	T_2 to T_3=2 mo
	T_3	58	100	76	88	5.24	6.55	112.9	0.97	88/109.5	0.804(4)	(3.55% increase)

* Data from McAdam and Cureton unpublished data. The equation used for peripheral resistance is essentially the same as given by Wiggers in "Cardiac Dynamics." Henry uses the same but quotes the early work of Wezler and Boger. P_m = mean blood pressure sitting (or the average of lying and standing), including the sum of systolic and diastolic pressures divided by 2; V_s = stroke volume by Grollman method with correction by Keys method, R = heart rate per second, and TPR = total peripheral resistance = $P_m/V_s \times R$.

† Used Keys' correction for absorption coefficient

‡ Used Keys' corrections for hyperventilation

In comparison with the comparable normal adult sample of men measured on the same 128 tests, 55 former champions, averaging 44.39 years of age, 69.37 in. (176.2 cm.) in height, and 165.29 lb. (76 kg.) in weight, were more mesomorphic, more linear in skeletal build and had less fat. The former champions also had slightly wider shoulders, smaller hips, and smaller gluteal and abdominal girths, they also had better feet, were found to have stronger dynamometer strengths, and scored better results in cardiovascular tests (better Barach, Schneider, and five-minute step test scores, better results in brachial sphygmograms, and higher T waves in precordial leads 4 and 5). The average weight residual of 17.05 lb. (8 kg.) was greater than that of the comparable sample of adults and even greater than the result for normal young men, indicating greater tissue density because these former champions were stronger and had less fat. Our external fat index correlates +0.70 with Benke's hydrostatic weighing determination of total fat.

The lying and standing blood pressures were just average by the tables for general adults, but the pulse rates were considerably lower. There was no indication that the former champions show relatively greater strain or deterioration, but they instead had significantly stronger circulation, greater vagus tone, and larger precordial deflections in the electrocardiogram. In the ratio of the area of the brachial pulse wave to the frontal area of the heart in diastolic phase (according to x-ray), the former champions showed greater proportionate stroke output per unit of heart size (3.489, compared to 2.599 for the comparable adult sample and 3.442 for young men). Their transverse heart diameters averaged 13.35 cm. (+4.73%), compared to 14.12 cm. for the comparable sample of adults and 13.1 cm. for normal young men (+0.60%). Comparison of the groups on an all-out step test for time and gross oxygen intake in the hard exercise showed the former champions to be superior to the comparable sample of the middle-aged, but both of these older groups were poorer in step-test time than the sample of young men. In gross oxygen intake the former champions were better than both other groups.

The former champions had a strength per pound of body weight of 7.09 compared to 6.54 and 5.87 for the other two groups respectively. The vertical jump reaction times were 0.271 seconds (visual), 0.254 (auditory), and 0.245 (combined). being about 5 in standard scores above the adult average, as were also the results for the agility run and vertical jump. However, both adult groups were considerably poorer in all-out chinning and dipping endurance exercise than the young men, but here again the former athletes had deteriorated less than the comparable sample of men. A division of the former champions into three subgroups designated "in continued training," "moderately active," and "sedentary" showed statistically significant differences in favor of the group in training over the other two groups in practically all physical fitness test items.

Untreated Factors

No attempt has been made to cover all that could be said about psychological factors or sex or racial differences. I am conscious of this omission, but these factors must be treated in subsequent articles. Most of all, each event has its own special mechanics, psychological mind-set (motivation), weather conditions, and timing. No single event has been adequately covered, nor has the long-range effect of each sport.

Because of space limitations, a bibliography has been omitted from THE JOURNAL and will appear in the author's reprints.

FOREIGN LETTERS

BRAZIL

New Method of Closure of Abdominal Wall.—Dr. A. J. Silveira and co-workers reported in *Revista paulista de medicina* (49:54, 1956) a new method of closure of the abdominal wall, which they have used in 101 operations with good results concerning suppuration and dehiscence. The suture of the fascia is made with a removable nickel-chromium thread, which they were the first to use. The suture of the fascia is made in zigzag, and the thread is put under tension, externally, by means of a metallic extending bar devised by Dr. Silveira. Metallic threads were preferred because sutures of vegetable or animal origin have crevices and gaps in their structure that favor the proliferation of germs, while the metallic threads are uniformly compact. For hemostasis the authors relied on vascular torsion, keeping all bleeders clamped during the operation, and the use of a U-shaped stitch that is removable through the skin. The extending bar and the metallic threads are removed eight days after the operation. Two of the patients in this series had to be operated on sometime after the first operation, at which time a firm aponeurotic scar was found. There were no eventrations in this series, and suppuration developed in only two patients, both of whom had had a cesarean section. In both of them, the poor preoperative condition of the patient could explain the occurrence of suppuration.

Arteriovenous Malformations.—Dr. M. P. Albernaz presented to the Associação paulista de medicina three cases of arteriovenous malformations in the region of the vertebral artery. Cerebral arteriography now permits the neurosurgeon to recognize arteriovenous malformations, which formerly were seen only at autopsy. The first patient had an arteriovenous malformation of the right posterior cerebral artery, and the second had an intrabulbar lesion. In both these patients the blood supply was maintained entirely by the vertebral system. The third patient had a great malformation of the region of the third ventricle, receiving blood from the right and left carotid systems but mainly from the basilar trunk. The first patient refused operation, the second died during the extirpation of the lesion, and in the third the lesion was considered inoperable. In this last patient the fractional pneumoencephalography was of great help in localizing the lesion.

Blastomycotic Tumor of the Femur.—Maffei and Hungria reported, in *Arquivos dos Hospitals da Santa Casa de São Paulo* (2:52, 1956), their findings in a patient with blastomycosis. One unusual finding was the presence of a solitary osseous lesion in the neck of the femur with no symptoms referable to it. Another was the presence of an osseous abscess that was sterile in the common culture mediums. The radiologist described the lesion as localized, destructive, and extra-articular without periosteal reaction or surrounding decalcification. Metastatic carcinoma, syphilitic gumma, osteoarticular tuberculosis, sarcoidosis (Boeck's sarcoid), osseous cyst, giant-cell tumor, plasma-cell (multiple) myeloma, Ewing's sarcoma, and chronic localized osteomyelitis had to be ruled out. The diagnosis was finally made by demonstrating the parasite by direct microscopic examination of the pus and in a biopsy specimen. Blastomycosis may give rise to a localized (hypergic) or a disseminated (anergic) reaction. The former is an inflammatory process with a granulomatous reaction due to the maximal fixation of antigen by antibody; the latter is a nonspecific necrosis with little or no cellular reaction. The treatment depends on the type of reaction. Sulfonamides are valueless and carry the danger of leukopenia and agranulocytosis, which occurred in the case reported. In localized lesions such as were seen in the authors' patient, complete excision is indicated. The patient was operated on and recovered completely.

Effects of Hysterectomy on Ovarian Function.—Dr. J. Gomes da Silveira and co-workers reported in *Revista de ginecologia e d'obstetricia* (98:515, 1956) that certain changes of vaginal cytology and ovarian structure followed hysterectomy in a group of adult rats. An identical study was made on women in whom vaginal smears were obtained before and after hysterectomy. The preoperative and postoperative rates of urinary elimination of gonadotropins, pregnandiol, and 17-ketosteroids were also compared. In some of these women subjected to a second operation but in whom the ovaries were intact, a biopsy specimen of these organs was taken. Several dogs were also subjected to hysterectomy and the ovaries examined from four to eight months after the operation. The authors' findings were as follows. 1. In adult rats hysterectomy did not cause immediate alterations in the curves of vaginal cytology that could be simply attributed to the absence of the endometrium, but it did determine late changes that corresponded to structural alterations of the ovaries, such as those found in the ovaries of women and dogs on whom hysterectomy had been performed. 2. In women hysterectomy brought about in general the symptoms of hyperfolliculinemia, corresponding to the great changes of the ovaries, but no significant modifications of the rate of urinary elimination of gonadotropins, pregnandiol, and 17-ketosteroids.

INDIA

Busulfan in the Treatment of Leukemia.—J. B. Chatterjea and co-workers (*Bulletin of the Calcutta School of Tropical Medicine*, July, 1956) used busulfan in the treatment of 11 patients with chronic granulocytic leukemia with encouraging results. Depending on the leukocyte count, the dose varied from 4 to 12 mg. daily and was gradually reduced to a maintenance dose of 2 mg. daily or on alternate days. In four patients it was the only drug used, and in two it was given during a relapse after initial treatment with deep x-ray and urethan. In the remaining five patients it was given in smaller dosage at a time when a relapse was imminent after deep x-ray treatment. In the first group, there was satisfactory hematological improvement, with regression of the size of the spleen and improvement in general condition. In the second group, the leukocyte count came down and the general condition improved. In the third group, the drug immediately controlled the proliferative disorder, and the blood findings and clinical condition reverted almost to normal. No toxic symptoms were noted. Busulfan appears to be the drug of choice in the treatment of chronic granulocytic leukemia.

Leprosy.—Fletcher and Shiralkar reported the results of treatment with Avlosulfon in 15 hospitalized patients with leprosy in *Leprosy in India* for April. The drug is given intramuscularly. Of the 15 patients, 12 had the lepromatous form, 2 had a borderline infection, and 1 had the tuberculoid form. All gave strongly

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The items in these letters are contributed by regular correspondents in the various foreign countries.

positive skin reactions at the commencement of treatment except the patient with tuberculoid leprosy, whose reaction was only slightly positive. Initially the dose was 50 mg. a week, but it was gradually increased to 200 mg. a week. No side-reactions were observed, except for pain in a few patients. All the patients improved clinically except the one with tuberculoid leprosy. Bacteriologically, 3 became negative, 2 were doubtful, and in the remaining 10 the bacillary count was greatly reduced. There was no deterioration in the hemoglobin level in most of the patients. The results compared favorably with those obtained by others with the same drug. The reduction in the quantity of medicine used, the simplicity of its preparation, the effective control over the dose taken by the patients, the absence of complications, and sureness of action are the chief advantages of the use of this drug.

Gandhi Medical College.—The foundation stone of a Gandhi Medical College building was laid at Bhopal in September by the Home Minister, who said that the establishment of the medical college was a welcome step, as the number of such institutions in the country was inadequate. Even if the present number was increased twentyfold, there would still be a need for more colleges. He hoped that medical facilities would be brought within the reach of every citizen, but he cautioned against opening understaffed and ill-equipped institutions.

World Health Organization Regional Committee.—The regional committee of the World Health Organization for Southeast Asia held its ninth meeting in New Delhi in September. Nearly 200 health projects to be carried out by member governments in 1958 were approved. In addition to delegates from Afghanistan, Burma, Ceylon, India, Indonesia, Nepal, Portugal, Thailand, and the United Kingdom, representatives of the United Nations, International Labor Organization, Food and Agricultural Organization, UNESCO, UNICEF, and the U. N. Technical Assistance Board also attended the meeting. The projects approved by the committee relate to the control of communicable diseases, maternal and child health, environmental sanitation, and training of medical personnel. The committee also formulated recommendations for the development of school health programs and accepted in principle an integrated plan for the eradication of malaria in Southeast Asia by 1961.

IRELAND

Voluntary Health Insurance.—Recommendations have been made to the Minister of Health of Eire for a voluntary health insurance plan for the whole country. Unlike Britain, Eire has no national health service covering all income groups. Free or partly free treatment is available only to the lower-paid workers. An insurance plan to cover the cost of hospital and medical, surgical, and maternity specialist services, but not treatment by general practitioners, is considered possible. Drugs and medicines would also be included if a proportion of the cost were paid by the insured person. Examples of minimum benefit rates are as follows: up to $20 weekly for hospital or clinical maintenance for a maximum of 10 weeks; from $20 for minor operations to $70 for major ones, and from $3 to $9 for anesthetics. Benefits for other services and drugs are also given, with limits for any one year. The annual premium would be $11.20 for an adult and nearly $4 for a child. Increasing the adult premium to $13.30 would make possible a maternity benefit of $56. Tax relief could be claimed on the premiums. The plan will probably be administered by a nonprofit organization backed by the government. Voluntary health insurance exists in Eire, but only on a limited scale and not through the normal commercial insurance companies.

JAPAN

The Japanese Diet.—Although the government announced a large surplus of rice, it cut the quotas in certain categories. For example, whereas a man doing hard labor such as mining coal used to get 600 gm. per day, his allotment has been cut to 400 gm., the same as everybody else, and, whereas there was formerly a slight increase for teenagers and middle-aged persons, they too get 400 gm. a day under the new quota. Japan has to import 6,500,000 tons of rice annually, or more than 25% of her total requirement. Prior to World War II, importations from Korea and Formosa sufficed, but now most of her imported rice comes from the United States. The introduction of wheat flour in the form of noodles and bread to relieve the rice shortage is proceeding rapidly under government sponsorship, though not rapidly enough. Superstitious belief still persists that rice has dietary factors not found in any other grain. Unfortunately, the polished rice eaten in Japan is so deficient in dietary requirements that it is common to find children with pot belly, anemic pallor, and bow legs. Since the children are almost entirely breast fed, the mothers' inadequate diet is reflected in the children. Many people eat no meat. While more fresh milk is being consumed due to the expanding dairy industry, no uniform standard prevails and the fat content of the milk varies widely. A strict government inspection of milk supplies appears to be still some distance away.

Nagasaki and the Atom Bomb.—On Aug. 9, the city of Nagasaki commemorated the 11th anniversary of its atomic explosion. Sixteen nations were represented, including Russia, Red China, and their satellites. There were the usual denunciations of the use of atomic weapons in war. A public announcement was made of the death of a 14-year-old girl, allegedly a victim of the atom bomb when she was 3 years old. At the time of exposure she showed no skin lesion or any other harmful effects save some superficial cuts from broken glass. She was apparently normal in every way until a year ago, when she began to complain of generalized weakness. The cause of her death was officially given as granulocytic leukemia due to exposure to atomic radiation. She was the 12th such victim to be reported this year. Japan still has over 6,000 living victims. The government has appropriated an additional sum of one million dollars to augment the effort to give them proper medical aid.

NORWAY

Carbutamide.—Dr. S. Aarseth reports on the treatment of 16 diabetics with carbutamide (*Tidsskrift for den norske laegeforening*, Sept., 1956). In nine patients the response was satisfactory. The patients who responded best were middle-aged or elderly, particularly those who were obese and whose disease was mild. As the diabetes is often a combination of different types, it may be difficult to anticipate the reaction of a given patient to this drug. It does not replace insulin, nor does it eliminate the need for dietetic measures. It works only if insulin is present in the body. Though disappointments were frequent with young patients, they were not the rule, and in a 13-year-old diabetic girl, complete normalization of the blood sugar level was achieved with the drug. Attempts to readjust by means of carbutamide the blood sugar level of diabetics whose disease is already stabilized by insulin revealed the risk of provoking acidosis and coma. Hence the author recommends confining any such attempt to the hospital. Diabetic acidosis and coma are contraindications to the use of carbutamide, which is ineffective in patients with these conditions. It should also be withheld in the presence of other acute complications of diabetes. Allergic skin reactions and renal insufficiency are also contraindications. Before trying carbutamide the patient should give a weight-reducing diet a fair chance. The treatment of diabetes with carbutamide is still experimental.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

The Number of Blood Cultures Necessary to Diagnose Most Cases of Bacterial Endocarditis. J. Belli and B. A. Waisbren. Am. J. M. Sc. 232:284-288 (Sept.) 1956 [Philadelphia].

The records of 82 patients with bacteriologically proved bacterial endocarditis who were seen at the Milwaukee County General Hospital between 1938 and 1954 were examined to determine how many blood specimens had to be drawn before a positive blood culture result was obtained. The ages of the patients ranged from 16 to 71; 20 were women and 62 men. The causative organism was Streptococcus viridans in 35 cases, nonhemolytic streptococci in 15, and Micrococcus pyogenes in 28. Other organisms were found in four cases. Three of the patients infected with Str. viridans and eight of those infected with other bacteria had received penicillin prior to the time the first blood was drawn. In 77 of the 82 patients the first positive blood culture was obtained within the first five cultures. Fifty-two of the cases were diagnosed by the first sample drawn. In no cases were more than 10 cultures needed to make the diagnosis. Forty-one per cent of all samples drawn had positive cultures. This study indicates that after five sterile blood cultures the possibility of making a bacteriologically proved diagnosis of subacute bacterial endocarditis decreases. Under these circumstances it is justifiable, therefore, to begin therapy in order to reduce valve damage and other complications of this disease.

Prolonged Use of Arterenol for Shock Following Myocardial Infarction with Patient Survival. I. S. Siglin. A. M. A. Arch. Int. Med. 98:372-376 (Sept.) 1956 [Chicago].

The author describes the case of a 52-year-old woman in whom emotional trauma precipitated a severe myocardial infarction at a time when her status anginosus seemed relatively well controlled. For one week after the infarction the patient presented a gradually progressive shock-like picture. Treatment with 16 mg. of levarterenol (Levophed) bitartrate in 1 liter of 5% dextrose in water by continuous intravenous drip was started when her blood pressure ran between 60/50 and 74/58 mm. Hg for over two hours despite intermittent intramuscular administration of vasopressors such as mephentermine. On the second day of the levarterenol therapy, which was continued for two weeks, severe pulmonary edema with loss of pulses and coma necessitated the use of tourniquets and positive-expiratory-pressure oxygen. The acute left heart failure lasted for six hours. One cubic centimeter of meralluride (Mercuhydrin) sodium was given intramuscularly and daily thereafter because of the pronounced dyspnea, orthopnea, pulmonary rales, and roentgen ray evidence of severe pulmonary congestion with marked cardiac enlargement.

After an initial dose of 100 mg. of cortisone given slowly intravenously on the fourth day of the levarterenol therapy, 25 mg. of cortisone was administered intramuscularly daily for one week. Levarterenol was withdrawn after a total dose of 402 mg. had been given in the course of 14 days. Drug fever apparently resulted from the administration of meralluride for 16 days but subsided after discontinuation of the mercurial therapy. Fever did not recur when mercaptomerin (Thiomerin) sodium was used as a diuretic. Thereafter recovery was slow but steady. After six months, the size of the patient's heart had returned virtually to normal and the lungs were completely cleared. Two years later, the patient led a normal existence, with only a rare anginal attack precipitated by emotional upsets or by walking in cold weather against a strong wind.

The gradually progressive shock-like picture with heart failure was reversed after 14 days of continuous sympathomimetic stimulation with levarterenol along with 7 days of corticosteroid therapy. The difference between failure and success in treating shock rests with early treatment before irreversible changes occur. This requires close observation of the patient and a change from frequent intramuscular injections of vasoconstrictors to continuous intravenous levarterenol drip with its greater ease of pressure control, as soon as it becomes impossible to maintain an adequate blood pressure by intermittent therapy. Since levarterenol apparently does not increase myocardial irritability, it may be that earlier use of this potent vasoconstrictor before frank evidence of vascular collapse sets in might increase the salvage rate in severe hypotension associated with myocardial infarction. Decrease in urinary output may be used as an indicator for strenuous antishock therapy in border-line cases of clinical shock. Constant care to see that the levarterenol solution does not escape from the vein is necessary.

Cortisone and Cortisone-like Substances in the Treatment of Tuberculous Meningitis. I. Santopadre and G. Silanos. Minerva med. 47:468-473 (Aug. 29) 1956 (In Italian) [Turin, Italy].

Fifty-one patients with tuberculous meningitis were treated with cortisone and cortisone-like substances in addition to the classic therapy of alternated cycles of streptomycin and isoniazid. This treatment was given at once or within 10 days to 30 patients; in the other 21 hormones were added to the antibiotics as soon as the condition of the patients made it possible. The hormone was given either orally or by injection in courses of 20 to 25 days each. Beginning doses of cortisone were 100 mg. for adults, 50 mg. for children, and 15 to 20 mg. for sucklings. Beginning doses of prednisone and prednisolone were: 30 mg. for adults, 15 mg. for children, and 10 to 15 mg. for sucklings. The doses were diminished progressively until the suspension of the treatment. The effects of the treatment on the general condition of the patients were very good. Comatose and precomatose forms were favorably influenced. Fever was checked and in some cases the temperature fell to almost critically low values. A high protein level in the spinal fluid and the occurrence of spinal fluid block were noticed. Hydrocortisone administered by spinal injection gave very good results. Paralysis of the cranial nerves was markedly affected. Untoward side-effects were not observed.

Subacute Thyroiditis: Report of Three Cases Treated with Cortisone. A. Moldover. A. M. A. Arch. Int. Med. 98:322-327 (Sept.) 1956 [Chicago].

Subacute thyroiditis is known under several names, such as de Quervain's acute recurrent, pseudotuberculous, and giant-cell thyroiditis. The term subacute thydroiditis, which is the term most frequently used today, distinguishes subacute thyroiditis from the suppurative and nonsuppurative forms, which last only a few days, and the chronic forms, Hashimoto's and Riedel's struma, to which it is not related. The author reports his observations on three patients with subacute thyroiditis and on one patient with carcinoma of the thyroid that closely mimicked thyroiditis. In the first patient, a 41-year-old woman, subacute thyroiditis was at first not recognized. The first symptom was severe pain at the base of the throat radiating to the left side of the neck, head, and ear. At the same time she had a short dry cough. Three weeks later she had temperature rising from 100 F (37.8 C) in the morning to 102 F (38.9 C) in the afternoon. She was treated with penicillin and oxytetracyline (Terramycin), but after two weeks the fever remained unchanged. The thyroid was symmetrically enlarged, firm, and exquisitely tender. She had tachycardia and some enlarged nodes in the axillas. She was hospitalized and was given daily, for 12 days, 150 mg. of propylthiouracil without any effect.

The place of publication of the periodicals appears in brackets preceding each abstract.

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After that, 25 mg. of corticotropin was given for 10 days, and then it was replaced by cortisone. It is not likely that the duration of the disease was shortened by cortisone. However, by the administration of cortisone the patient was kept symptom-free and able to continue her normal activities, whereas without this medication she might well have been invalided during the entire period. The return of symptoms on premature cessation or reduction of the dose of cortisone emphasizes the importance of continuous therapy until signs of the disease (tenderness and enlargement of the gland, elevated sedimentation rate) have disappeared. In the second patient there was immediate response to cortisone. The third patient had creeping or migrating thyroiditis, in which at first only one lobe is involved and later the other lobe becomes enlarged and tender. The disease ran its usual course, but with cortisone the temperature came down to normal and all the symptoms disappeared within a few days instead of weeks or months. Subacute thyroiditis may be confused with carcinoma, but the two conditions can be differentiated by watching the effect of the administration of cortisone for two or three days.

Analysis of Bronchoscopic Report in 185 Cases of Bronchial Carcinoma. A. E. Paletto, E. Masenti and F. Viglione. Minerva med. 47:342-348 (Aug. 11) 1956 (In Italian) [Turin, Italy].

The authors report bronchoscopic findings in 185 cases of bronchial carcinoma. Bronchoscopic appearances and pathological findings obtained from the removed tissue were compared. Patients were divided into three groups. The first group was characterized by the presence of neoplastic tissue and ulcerations that were directly visible. To the second group belonged patients in whom the bronchial morphology had been markedly altered by the disease. These alterations resulted in stenosis, rigidity, hypomobility, and deformity. To the third group belonged patients whose bronchoscopic findings were negative or in whom manifestations of an inflammatory type were present.

Histological diagnosis based on biopsy was positive in 110 cases (59%), probable in 66 (35%), and negative in 18. Endoscopic examination is quite reliable in indicating whether a patient should be operated on. Comparison of the bronchoscopic and the pathological findings showed that in the patients of the first group the neoplastic infiltration was the same as that detected by bronchoscopy; in the second and third groups the spread of the tumor was much wider than that indicated by bronchoscopy. Early symptoms in relation to the bronchial syndrome of irritation did not indicate any substantial differences between the three groups. The symptoms had lasted longer in patients of the first group than in those of the second and third groups.

Evaluation of Adrenal Cortical Function by Stimulation with Corticotropin (ACTH). N. H. Engbring, R. B. Truitt and W. W. Engstrom. A. M. A. Arch. Int. Med. 98:257-265 (Sept.) 1956 [Chicago].

Determining the concentration of steroids in urine or blood frequently fails to differentiate patients with adrenal insufficiency from those with intact adrenals. The capacity of the adrenal cortex to respond to stimulation was tested by combining the administration of corticotropin with methods that measure the concentration of adrenal hormone. Administration of from 20 to 25 U. S. P. units of corticotropin in a dextrose solution over a period of from 5 to 10 hours will evoke a maximal response in adrenal cortical function during the period of infusion that will be reflected in the urinary steroid excretion. A single infusion may be sufficient to establish the integrity of the gland, or repeated infusions on three or more successive days may be necessary before an unequivocal rise in urinary steroids is observed. With the introduction of more uniformly potent preparations of repository corticotropin, which can be given intramuscularly and which are capable of causing prolonged adrenal cortical stimulation, a simpler technique became available. The results obtained from testing with these preparations were compared with those obtained with the intravenously administered corticotropin. Corticotropin was given intravenously to 35 patients and the long-acting intramuscular corticotropin to 22 patients. Most of the patients had chronic illnesses. In a few instances the studies were made to exclude a diagnosis of Addison's disease, which had been suspected from clinical or other laboratory evidence; further follow-up disproved the existence of adrenal insufficiency. Some of the tests were made to determine the response in patients with relatively acute or self-limited disorders. Since patients with acute, and especially those with chronic, illnesses are the persons in whom it is most difficult to exclude adrenal cortical insufficiency, and since in these the urinary steroid excretion is frequently depressed, it was felt that control studies should be performed on sick patients rather than on healthy persons. For comparison, similar tests were carried out on four patients with Addison's disease and six patients with anterior pituitary insufficiency.

Either of the two methods induced a significant rise (100% or greater if the control level was above 2 mg. and 200% or greater if the control value was very low, i. e., less than 2 mg.) in either the urinary 17-ketosteroids or the corticosteroids in 54 of 57 patients studied. When an insignificant rise occurred in one urinary fraction, there was usually a significant rise in the other, the corticosteroids being the more sensitive indicator of adrenal activity. The results obtained by the use of intramuscular repository corticotropin were more conclusive than those with intravenous corticotropin given over a period of five or six hours. No doubt much longer or continuous periods of infusion of intravenous corticotropin would have given better results, but the technique is inconvenient. The measurement of the increments in urinary steroids under the influence of corticotropin provides an accurate, safe, and direct test of gross adrenal cortical function. It is likely that tests of this nature will largely replace older tests for chronic adrenal cortical insufficiency, especially in patients with complicating illnesses. In view of the considerable individual variations in steroid output, it was not possible clearly to differentiate patients with known anterior pituitary insufficiency from sick patients with intact adrenal and pituitary function. Therefore, it is not likely that these techniques are sufficiently quantitative to detect "potential" adrenal cortical insufficiency, such as might be present in a person who has received hormone therapy.

Proctosigmoidoscopy in the General Physical Examination: An Analysis of 5,158 Examinations. E. L. Crumpacker, J. P. Baker, H. C. Ballou and others. A. M. A. Arch. Int. Med. 98:314-321 (Sept.) 1956 [Chicago].

A proctosigmoidoscopic examination is part of the general physical examination of male patients at the Greenbrier Clinic, a diagnostic medical clinic at which approximately two-thirds of the patients are examined under company-sponsored executive health programs. Proctosigmoidoscopy is performed by the internist. Most examinations are carried out in the morning. If the patient has had a morning bowel movement, frequently no further preparation is needed. If feces are encountered, a low enema of sodium biphosphate and sodium phosphate (Phospho-Soda) solution is administered. This results in excellent preparation in nearly all patients. An attempt was made to pass the sigmoidoscope as far as safely possible. Quite frequently it was impeded at 16 to 17 cm. by angulation or spasm of the colon. A total of 5,158 examinations were performed on 2,401 men. Rectal or sigmoidal polyps or both were discovered in 161 patients (6.7% of patients examined, 3.1% of the total examinations). As expected, polyps were most often discovered on the first examination (3.9%), but a high yield was also obtained on the second annual examination. Thereafter, there was an almost constant finding of slightly more than 2% on each subsequent annual examination. In 113 instances the polyps were solitary, but in 48 from two to "many" were observed. They were located from 3 to 25 cm. from the anal margin; only 40 (25%) were less than 10 cm. from the anus; and only four were felt on digital examination of the rectum. Seventeen (10.6%) of the 161 patients gave a history of rectal bleeding.

All patients with polyps were urged to consult a proctologist for removal of the neoplasms. Since many surgeons fulgurate small polyps without biopsy, the authors received pathological reports in only 53 instances; 36 were said to be benign adenomatous polyps; 8 contained invasive carcinoma; 8 others were reported as carcinoma in situ, hyperplastic polyps, or atypical hyperplasia; one was a carcinoid. Three cases of previously unsuspected multiple polyposis of the colon were discovered by the combination of routine proctosigmoidoscopy with follow-up double-contrast barium-enema studies. Carcinoma of the rectum or colon often develops from benign adenomatous polyps. Digital examination and barium-enema studies will demonstrate a small percentage of rectal polyps, but only proctosigmoidoscopy can be relied upon. One in seven patients with rectal and sigmoidal polyps will have neoplasms at a higher level in the colon. Polyp detection is frequently cancer detection and more frequently cancer prevention. Proctosigmoidoscopy should be a part of every general examination of adults.

Mediterranean Anemia in an Adult Negro. J. E. Norris, H. H. Hanson and R. K. Loeffler. A. M. A. Arch. Int. Med. 98:356-364 (Sept.) 1956 [Chicago].

The authors describe a case of Mediterranean anemia in a 32-year-old Negro woman. She was completely asymptomatic until the age of 19 years, when splenomegaly was accidentally detected. Subsequently, she was gainfully employed, was not incapacitated, and was first seen at Herrmann Hospital in Houston, Texas, at the age of 32, because of acute biliary colic, jaundice, and menorrhagia. The menorrhagia contributed to her anemia and was relieved by hysterectomy. The subsequent course proved that a stone associated with acute biliary colic was the cause of the jaundice. Mediterranean anemia is not punctuated by hemolytic crises of this degree. Fourteen months after the hysterectomy she was readmitted to the hospital for acute pyelonephritis. Except at the time of these incidental complicating illnesses, the patient was unaffected by her anemia. The diagnosis of Mediterranean anemia was established by physical examination, erythrocyte hemoglobin analysis, and family studies. The patient was in good health, was gainfully employed, and was asymptomatic at a recent follow-up. Splenectomy was decided against, as the red cell survival was normal.

The fact that many persons with Mediterranean anemia lead a relatively asymptomatic normal existence is not well known, nor is it always realized that no race or age is exempt from this disease, although it is rare in Negroes. The consensus regarding the mode of inheritance of Mediterranean anemia is that the severe, fully developed syndrome is inherited as a single dominant gene variably expressed; thus, the homozygous form of the disease manifests itself in the severe classic anemia terminating fatally early in life, and the heterozygous form only in the characteristic changes in the erythrocytes causing no symptoms. Patients with the milder forms of the disease may survive through the fourth and fifth decades. Establishing the exact diagnosis in an adult Negro presents a major cooperative task. A study of the family and hemoglobin analysis are essential. The triad observed in the patient consisted of increased clearance rate, relatively high plasma iron concentration, and poor incorporation in circulating red cells. The same pattern was observed by the authors in five patients with severe Mediterranean anemia and in four patients with pernicious anemia. The fact that Mediterranean anemia is primarily a defect in hemoglobin synthesis and red cell production and not a hemolytic process interrupted by crises is emphasized.

Identification and Significance of Platelet Antibodies. J. L. Tullis. New England J. Med. 255:541-551 (Sept. 20) 1956 [Boston].

A simple method for the clinical demonstration of antiplatelet antibodies is described. Many cases of purpura, especially idiopathic thrombocytopenic purpura and hypersplenism, are due to the development of immune antiplatelet antibodies. The differentiation of these cases from non-antibody-induced purpura is of considerable clinical significance, chiefly because of new therapeutic agents: adrenocortical hormones and platelet transfusions. Thrombopenia secondary to deficient platelet production, as in metastatic cancer, leukemia, or radiation, generally is not on an antibody basis. Such cases respond best to platelet transfusions. Primary idiopathic thrombocytopenic purpura, hypersplenism, and neonatal purpura, on the other hand, are frequently due to the presence of circulating antiplatelet antibodies. Such cases respond best to splenectomy or adrenocortical hormones or both. The transfusion of platelets, in these cases, could theoretically lead to an aggravation of the underlying disorder. The test consists of a simple mixture of preserved platelets (as antigen), unknown serum (as antibody), and a small amount of human complement. The mixture is incubated at 37 C and studied at 45 and 90 minutes. Normal serum incubated in this manner will cause little or no decrease in platelet count, whereas serum containing platelet antibodies will cause a decrease in count secondary to agglutination or lysis or both. The test serum is treated to remove all components of the coagulation system before addition to the incubation mixture. The antibody titer remains essentially unaffected by this treatment. As a result of this treatment, any subsequent interaction between platelets and serum can be ascribed to antigen-antibody reactions. A normal control serum is tested simultaneously as a standard.

The test requires no elaborate equipment, but scrupulous attention must be paid to the proper preparation of the serum and performance of the platelet counts to give reliable results. Use of this test as a screening procedure in diverse thrombopenic and hemorrhagic disorders revealed that in 57% of all patients with idiopathic thrombopenic purpura, 66% of all patients with hypersplenism, and 60% of all patients with neonatal purpura tested in this series the disease was due to circulating antiplatelet antibodies. Secondary thrombopenic purpura does not give rise to a positive antibody test except in rare cases. The finding of a positive antiplatelet-antibody test result in an undiagnosed case of thrombopenic purpura is strong evidence against the presence of obscure leukemia or metastatic cancer. The serum factor that gives rise to antiplatelet-antibody tests can be shown to be an antibody by immunologic and chemical tests.

A Family Epidemic of Psittacosis with Occurrence of a Fatal Case. R. L. Prouty and W. S. Jordan Jr. A. M. A. Arch. Int. Med. 98:365-371 (Sept.) 1956 [Chicago].

The authors describe four cases of psittacosis occurring in a family of 12 persons consisting of a 40-year-old Negro minister, his 37-year-old wife, and their 10 children between the ages of 2 and 18 years, who were exposed to two apparently healthy parakeets. This family epidemic of psittacosis resulted in the death of the father and infection of the mother and two children aged 16 and 18 years, with manifestations ranging from severe illness to mild symptoms. Three of the four patients with symptoms had serologic evidence of psittacosis. A diagnostic antibody titer was found in the serum of a fifth member of the family, a 10-year-old boy who had cleaned the bird cage only once. The cage was usually cleaned by his 14-year-old brother, who, despite his more intimate contact with the birds, had neither symptoms nor antibodies. The remaining six members of the family also did not have symptoms or antibodies.

Psittacosis viruses were isolated from the lungs of the patient who died and from one of three parakeets obtained from the store in which the two birds given to the family were purchased The increasing number of cases of psittacosis in humans calls for a reconsideration of control measures, including education of the public and legislation regulating the importation and sale of psittacine birds.

Causes, Origin and Prevention of Endemic Goiter. H. J. Wespi Munchen. med. Wchnschr. 98:1150-1157 (Aug. 31) 1956 (In German) [Munich, Germany].

Of the two types of endemic goiter, i. e., the diffuse and the nodular, the first occurs most frequently in newborn infants, children, and adolescents. While nodular goiter, as a rule, is not reversible, diffuse goiter shows a satisfactory response to the administration of iodine. The author's observations at the gynecologic clinic in Zurich and at the department of obstetrics and gynecology of the Canton Hospital in Aarau, Switzerland, convinced him that it is in newborn infants that normalization of the condition of the thyroid gland by adequate iodine prophylaxis is manifested most rapidly. The supply of iodized salt (with the dose of iodine varying from 5 mg. to 20 mg. of potassium iodide per kilogram of salt) to pregnant women resulted in the reduction of the incidence of goiter in newborn infants from 20.7% (without iodine prophylaxis) to 6.4% (with a dose of 5 mg. of potassium iodide) and to 2.6% (with a dose of 20 mg. of potassium iodide).

An addition of 5 mg. of potassium iodide to each kilogram of salt used not only for cooking purposes but also in bakeries, butcher shops, and for cattle feeding, was introduced gradually in all the cantons of Switzerland between 1922 and 1940, and only in a few of them was the iodine dose increased to 10 mg. of potassium iodide per kilogram of salt on the recommendation of the government. As a result of this general measure endemic goiter practically disappeared, not only in the newborn infants but also in school children and in adolescents. While in the first two decades of the 20th century up to 65 of each 1,000 recruits had been found unfit for active military service, this incidence was reduced to 39 per 1,000 in 1923; a further decrease occurred continuously to 1 per 1,000 in 1940 and to even less in the following years. In addition to the reduced incidence of endemic goiter, the incidence of its complications, including cretinism and deaf-mutism, was also reduced considerably. The number of deaf-mutes dropped from 12 to 16 among 10,000 children born in 1922 to 4 to 6 among 10,000 children born in the period between 1940 and 1945, and of these deaf-mutes not one was a cretin. Despite the introduction of iodized salt used for cooking purposes as a general measure, the incidence of toxic diffuse goiter or of hyperthyreosis was not increased but rather somewhat reduced in Switzerland. Exogenous iodine deficiency is considered the main factor in the origin of endemic goiter. Consequently, a sufficient supply and uptake of iodine must be secured for its prevention. The addition of iodine to the salt used for cooking purposes in doses that ensure a daily supply of from 100 to 200 gammas of iodine, regulated according to local eating habits, is recommended as a simple, safe, and harmless means for the prevention of goiter in endemic areas.

Hemorrhagic Thrombocythemia: A Blood Coagulation Disorder. T. H. Spaet, S. Bauer, and S. Melamed. A. M. A. Arch. Int. Med. 98:377-383 (Sept.) 1956 [Chicago].

The authors report hemorrhagic thrombocythemia resulting from polycythemia vera in a 71-year-old woman. In the course of five years the patient had repeated episodes of gastrointestinal bleeding and other hemorrhagic manifestations, such as massive, spontaneous epistaxis, many of which were treated with blood transfusions. Two 1,000-r courses of x-ray therapy were given to the gastric area in an attempt to reduce gastric acidity. Once, whole body irradiation, 35 r, was given to depress the blood platelets. For almost two years after this treatment the patient appeared to be relatively free of hemorrhage. Except for this period, the course of the disease was characterized by a persistent elevation of blood leukocytes and generally an increase in platelets reaching 10 million per cubic millimeter. The blood coagulation time, prothrombin, prothrombin consumption, fibrinogen, and clot retraction were all normal. The heparin clotting time was found to be definitely shortened. The patient's platelets displayed anticoagulant activity in the thromboplastin generation test when used at circulating levels but behaved normally when diluted to normal levels. Normal platelets were similarly anticoagulant when concentrated to thrombocytothemic concentrations. It is suggested that the fundamental defect in hemorrhagic thrombocythemia is a coagulation disorder resulting from the anticoagulant effect of excess platelets.

When the patient's platelet count had again risen to about 2 million per cubic millimeter and the hematocrit was up to 58 per 100 cc., she was given 4 mc. of radioactive phosphorus (P^{32}) intravenously. In addition, 500 cc. of blood was removed by venesection. Within a month the platelets had fallen to normal levels, where they had remained to the time of the writing of the paper (four months after the administration of the P^{32}). No further hemorrhagic episodes have occurred.

SURGERY

Bilateral Resection in Pulmonary Tuberculosis. A. Falk and N. K. Jensen. Am. Rev. Tuberc. 74:367-375 (Sept.) 1956 [New York].

Falk and Jensen report observations on 60 patients who underwent bilateral pulmonary resections. These 120 (60 bilateral) resections represent approximately one-fourth of all resections carried out between February, 1951, and July, 1955. The very low operative mortality, freedom from complications, and good clinical results in patients with unilateral resections, who had received preoperative antimicrobial therapy for four months or more, led to consideration of the possibility of bilateral lung resection, particularly for patients with known cavitary disease and persistently infectious sputum. Patients selected for bilateral resection included first, patients whose sputum and gastric washings contained tubercle bacilli, who had persistent cavitation, or who had roentgenographic evidence of instability of the lesions after six months or more of chemotherapy. A second category included those with residual disease, particularly if it was allied with atelectasis, fibrosis, or some other destructive process in the lung. Men who are just beginning their life-work or those established in occupations and with family responsibilities (usually less than 50 years of age) should have the advantage of resection to avoid possible future relapse. Public health risks, and the patient who continues to discharge tubercle bacilli in the sputum, were considered for bilateral resection because it provided these patients with the possibility of returning to their homes or communities without the restrictions or stigma of the "good chronic." Resectional therapy also offered to the patient without a home or family the possibility of living in a domiciliary or other arrangement outside the hospital, with obvious social benefits for the individual and a considerable saving in the cost of hospital care.

All 60 patients were white men ranging in age from 20 to 58 years. Forty-six of the patients were less than 40 years old. There were 31 patients with moderately advanced and 29 with far-advanced disease at the beginning of chemotherapy. Far-advanced disease was more frequent in the group under 40 than in the older age groups. The duration of preoperative chemotherapy varied from 1 to 19 months, with the largest number of patients receiving from 5 to 8 months of therapy. The group receiving more than one year of preoperative chemotherapy consisted, with one exception, of those with far-advanced disease. After surgery chemotherapy was continued for a minimum of six months. Since 1954, the minimum total duration of chemotherapy in the resection series has been 18 months. Judging from the incidence of postoperative complications (28 in 120), bilateral resection carries no unusual or added risks. Only three of the 60 patients continued to discharge tubercle bacilli after the second resection. Two of these patients had a postoperative bronchopleural fistula, which healed slowly. Both were also known to have tubercle bacilli resistant to several antimicrobial agents. The third patient had residual tuberculous bronchitis and saccular bronchiectasis of the remaining lung segments. All three now have had sputum cultures free from tubercle bacilli for six months or more. There were no bacteriological or roentgenographic relapses in any of the remaining 57 patients after the second resection and initial sputum conversion. Bilateral resection offers an additional therapeutic approach in selected cases in which sputum conversion has not been achieved by other methods of therapy.

End-to-Side Bypass Homograft Without Resection in Segmental Arterial Occlusion. H. Laufman, R. Hohf, V. Bernhard and O. Trippel. A. M. A. Arch. Surg. 73:418-431 (Sept.) 1956 [Chicago].

The authors performed 19 bypass procedures upon 17 extremities in 15 patients. The patients ranged in age from 46 to 69, and all but one were men. In each instance the indication for surgery was intermittent claudication or ischemic pain of other types associated with an impalpable pulse distal to the occlusion. One patient had gangrene of the great toe. The occlusion was in the femoral artery in 16 extremities, in the iliac artery in 2, and in the iliac-femoral-popliteal in 1. The pathological process in every case was occlusive arteriosclerotic disease. Arteriography was done by the transaortic route in about one-third of the patients and retrograde through a pulsating femoral artery in two-thirds. The occlusions varied from 2.5 cm. in length to total absence of a lumen from the aortic bifurcation to the popliteal artery. The vast majority occurred in the femoral artery. The distal run-off was estimated as poor in two extremities and fair in three. The remaining extremities appeared to have an adequate distal vascular bed.

The authors applied the bypass technique to short as well as to long arterial occlusions on the premise that anastomoses can thus be made far enough away from the occlusion proximally and distally to assure working with the best possible arterial wall in the host, and with minimal dissection. Furthermore, in an effort to establish the limitations of the procedure, they performed it in certain borderline cases in which the peripheral vascular bed was of questionable patency. The end-to-side bypass lends itself readily to virtually any type of segmental arterial occlusion in the lower extremity. Selection of patients with adequate peripheral run-off appears to be of prime importance, although many with less than adequate distal circulation obtain some benefit. Some of these patients recover a distal pulse but develop postoperative edema of the foot and ankle. Immediate success in restoring distal pulsations was obtained in 15 of 19 bypass grafts. Four delayed failures occurred from six days to four months postoperatively, two as the result of delayed occlusion and two as the result of rupture. The circulatory status of the limb subjected to surgery was not worsened in any case, regardless of failure of a graft to function. There were no deaths. In some instances of failure to restore pulse to the ankle vessels, symptomatic improvement was seen nonetheless. Reoperation was carried out in two instances of failure, with one successful result.

Cardiospasm: Results of Heller's Operation. A. Gammelgaard, J. Iversen and G. Thomsen. Acta chir. scandinav. 111:98-107 (No. 2) 1956 (In English) [Stockholm, Sweden].

Twenty men and 14 women with cardiospasm underwent extramucosal myoesophagocardiotomy (Heller's operation) (35 operations) at the department of thoracic surgery of Rigshospitalet in Copenhagen, Denmark. The approach was by left thoracotomy in 32, by right thoracotomy in one, thoracoabdominal in one, and abdominal in one. There were no operative or postoperative complications except for an operative injury of the gastric mucosa sustained by one patient in the course of myotomy and repaired by suture. Thirty-one patients were followed up for an average of three and a half years. Fifteen patients (49%) obtained excellent results with no complaints, 11 patients (35%) had satisfactory results with only occasional retrosternal oppression on swallowing, and 5 patients (16%) had poor results with recurrence of dysphagia, retrosternal oppression, and rumination. Comparison of preoperative and postoperative roentgenograms revealed improvement in 24 patients, i. e., a gradual decrease in the degree of dilatation and a more rapid emptying through the cardia to the stomach. No regurgitation was observed. The poor results could be ascribed to concomitant disorders such as hiatal hernia, neurinoma in the stomach, epiphrenic hernia, and segmental esophageal spasm, or to technical faults. Heller's operation performed through a left-sided thoracotomy is a satisfactory solution of the surgical problem in cardiospasm, affording clinical improvement in practically all patients. An epiphrenic diverticulum developed during the myotomy in two patients, but it caused symptoms only in one.

Subtotal Gastrectomy for Peptic Ulcer: A Comprehensive Review of Two Hundred Thirty-Six Cases with Emphasis on the Treatment of the Ulcer Which Causes Obstruction. W. S. Caudell, C. Marshall Lee Jr. and C. A. Liebig. A. M. A. Arch. Surg. 73:469-480 (Sept.) 1956 [Chicago].

Caudell and associates present an analysis of 236 patients subjected to a subtotal gastrectomy for peptic ulcer during the five-year period from June, 1949, to June, 1954. A major objective of this analysis was to determine whether it is possible to anticipate technical difficulty before the intervention. It was found that technical difficulties could be correlated with the clinical findings. They were encountered in nearly 70% of the patients with duodenal obstruction or about twice as frequently as in any other group. The duodenal lumen was entered either intentionally or accidentally in 42% of the patients with duodenal obstruction or about four times as often as in patients with duodenal pain. The presence of significant obstruction in peptic ulcer should forewarn the surgeon of a difficult operative procedure and permit him to prepare for it.

The authors strongly endorse the medical management of peptic ulcer in suitable cases. The "conservative" method, however, was often unduly prolonged, to the serious disadvantage of the patient. If failures of medical management were recognized earlier and accepted as such, with a prompt decision in favor of surgical intervention, the incidence of technically difficult, high-risk cases could be substantially reduced. Special attention is given to the importance of adapting the surgical procedure to the needs of the individual patient. The fact that a patient has been scheduled for a subtotal gastrectomy does not necessarily mean that a portion of his stomach must be removed. Some surgeons consider a scheduled gastric resection as a sort of personal challenge to be completed at any cost, and thus probably contributes more than any other single factor to the complications of elective gastric surgery. Although methods of dissecting and closing the duodenal stump are as numerous as the techniques for reanastomosis of the gastrointestinal tract, no single procedure has proved satisfactory in all cases. Suggestions are offered to increase the safety of operations.

The Surgical Complications of Meckel's Diverticulum in Infants and Children: An Analysis of Sixty Cases. C. D. Benson and L. M. Linkner. A. M. A. Arch. Surg. 73:393-398 (Sept.) 1956 [Chicago].

Meckel's diverticulum or remnant of the vitelline duct may cause serious surgical complications in the pediatric age group. The authors reviewed the records of 60 children with such complications, ranging in age from 1 day to 14 years. Nearly one-third of the children were less than one year old, and 75% were under 5 years. The complications observed in this group, in the order of their frequency, were intestinal hemorrhage, abdominal pain, acute intestinal obstruction, umbilical fistula, and perforation with peritonitis. The parenteral administration of fluid and blood is essential to insure a high survival rate, particularly in the newborn and in infants. It is essential to restore the blood volume to near normal levels before attempting surgical treatment in patients in whom moderate to severe hemorrhage is the presenting symptom. The authors adhered to this principle in the 24 patients who had intestinal hemorrhage, and all of them survived.

Mechanical obstruction and intestinal hemorrhage are the most frequent surgical complications of Meckel's diverticulum in the first two years of life. With increasing age, intestinal hemorrhage and obstruction become less frequent but acute inflammation of the diverticulum occurs more often. There were four deaths, or a mortality rate of 6.7%, in the 60 infants and children operated on. All of the four patients who died had acute intestinal obstruction and a gangrenous intestine. Fifteen of the 18 patients who required intestinal resection and anastomosis survived.

Tuberculous Tenosynovitis of the Hand Treated by Combined Surgery and Chemotherapy. M. Fellander. Acta chir. scandinav. 111:142-150 (No. 2) 1956 (In English) [Stockholm, Sweden].

Eight men and 11 women between the ages of 19 and 70 years with tuberculous tenosynovitis of the hand were treated with complete surgical removal of the diseased tendon sheath combined with systemic and local chemotherapy. After excision of the synovial sheath and effective hemostasis, 1 gm. of streptomycin was applied locally. One gram of streptomycin was given intramuscularly once daily for from three to six weeks, or for longer periods in complicated cases. Ten to 14 gm. of aminosalicylic acid (PAS) and 0.3 to 0.4 gm. of isoniazid were given orally daily for the entire period of treatment. Relapses occurred in six patients, but complete recovery resulted from chemotherapy alone in one of these and from reoperation in five. Fourteen of the 19 patients were followed up for from three and one-half to five and one-half years after the first operation. In six of these patients the tenosynovitis involved the volar sheaths at the wrist, in three those on the fingers, and in five the dorsal sheaths at the wrist. No recurrences of the tenosynovitis were observed at follow-up. In one patient a tuberculous synovitis of the wrist developed two years after the operation. In all the other patients the recovery was complete, with a good functional result. The results obtained with combined surgery and chemotherapy were much better than those obtained by the author with both surgical and conservative treatment, and they were distinctly better than those reported in the literature before the advent of chemotherapy. It is advisable to begin treatment with combined chemotherapy for a short period and to observe the patient's response. If there is no response, it is advisable not to wait too long before operating. Otherwise there is danger that the tenosynovitis will spread to the adjacent joint and bone and that destruction of the tendons will occur.

Argentaffin Carcinomas: Report of Twenty-Nine Cases, Six Malignant. W. J. Eldred. A. M. A. Arch. Surg. 73:517-525 (Sept.) 1956 [Chicago].

Twenty-nine argentaffin carcinomas were collected from the postmortem records and surgical pathology files of San Francisco Hospital (University of California Service) and Franklin Hospital in San Francisco, representing the 23-year period from 1932 to 1954. Of these 29 cases, 24 are analyzed. Seventeen patients were treated surgically, and the tumors of the other 12 were found at autopsy. The author regards the term "carcinoid" tumor as undesirable and prefers the term argentaffin carcinoma. Ten of the 29 tumors were appendiceal tumors. Most authors report a higher incidence of these tumors in the appendix than elsewhere. The rest of the tumors were distributed in the gastrointestinal tract as follows: ileum, 9 cases; small intestine (unspecified), 3; rectum, 3; jejunum, 2; duodenum, 1; and cecum, 1. The appendiceal argentaffinoma is frequently found in an appendix removed for inflammation. Three of the present series of ten appendices were inflamed. Appendiceal argentaffin carcinomas have a good prognosis because the tumor is often obstructing and gives rise to symptoms. Thus, early surgery results in removal of the tumor and there is less likelihood of its having progressed to the stage of serosal and lymph node spread than is the case with an identical tumor situated elsewhere in the gastrointestinal tract.

Appendectomy with wide excision of the mesoappendix is the treatment recommended when an argentaffin tumor is found in the appendix. Intermittent obstruction of the small intestine or x-ray demonstration of a filling defect or kinking of the terminal ileum in a middle-aged patient should alert one to the diagnosis of argentaffin carcinoma. Another feature that may prove of diagnostic importance is the association of these tumors with valvular disease of the right side of the heart, sudden flushing of the skin, an unusual type of patchily distributed changing cyanosis, and "asthma." The cause of the syndrome is thought to be substances with vasoactive properties. Serotonin, or enteramine (5-hydroxytryptamine), is most likely to correspond with the signs and symptoms of the syndrome. Recently, it was extracted in considerable amounts from an argentaffinoma. Recognition of the vasomotor symptoms should result in more cases of argentaffin carcinoma being discovered and brought to operation. The radical surgical extirpation of such tumors is often followed by a relatively long and comfortable life for the patient. Removing the primary tumor in patients with extensive metastases often results in arrest of further metastases for several years.

Critically Crushed Chests: A New Method of Treatment with Continuous Mechanical Hyperventilation to Produce Alkalotic Apnea and Internal Pneumatic Stabilization. E. E. Avery, E. T. Mörch and D. W. Benson. J. Thoracic Surg. 32:291-311 (Sept.) 1956 [St. Louis].

Approximately 25% of deaths from traffic accidents are due to chest injuries. A number of patients with severe chest injuries who were rapidly failing with the usual modern means of treatment were quickly stabilized and eventually recovered by the use of continuous mechanical hyperventilation. The first patient treated by this method was a 51-year-old man who had been slowly rolled into an 8-in. space between a diesel locomotive and a steel furnace. He was admitted moribund, in deep shock, with multiple bilateral fractures of ribs; costochondral separations; bilateral tension hemopneumothorax; fractures of the sternum, clavicles, and pelvis; crushing injuries of the liver and genitourinary tract; paralytic ileus; and acute gastric dilatation. Bilateral intrapleural catheter water-trap drainage was carried out along with tracheotomy. The anterolateral chest wall was partially stabilized with soft tissue traction. Long metal pins were passed under the pectoralis and serratus anterior muscles on each side. Spreader bows were attached and traction applied to an overhead frame. Although the paradoxical motion was partially corrected, respiratory acidosis continued because of inadequate ventilation resulting from actual lung destruction and pulmonary edema. Various demand-flow and pressure-cycled respirators were tried, but these machines did not ventilate the patient adequately. The piston-type intermittent-positive-pressure respirator developed by Mörch was then applied, and the patient's condition improved from a semicomatose state of respiratory acidosis to a more alert state of alkalotic apnea. The pH was kept in a range of approximately 7.45. Lung inflation and deflation were mechanically maintained rhythmically and smoothly, with loss of all paradoxical motion. This stopped all overriding and grinding motions of the broken rib ends and promoted their healing. Soft tissue traction was discontinued as soon as it was realized that stabilization of the chest was to be obtained with mechanical ventilation. This was maintained for 30 days until the patient was able to breathe adequately without the assistance of the machine. The patient was discharged from the hospital 51 days after the injury and has returned to his work. The authors used the same principles of management in a number of other severe chest and combined head and chest injuries with equally good results.

The most striking benefit of this mechanical hyperventilation treatment is that it is safe and allows the survival of patients with a seemingly hopeless prognosis. Its chief advantages are correction of paradoxical motion of the chest wall; removal of hypoxia and hypercarbia; absence of pulmonary edema; less sedation is required; no serious deviations in blood chemistry with prolonged mild respiratory alkalosis; no measurable circulatory defects; prompt return of blood chemistry and physiological responses to normal with cessation of hyperventilation; and no late ill-effects. Continuous mechanical ventilation should be applied whenever the function of the chest wall has been impaired, as in crushing injuries of the chest; infections (poliomyelitis, tetanus); muscle disease (myasthenia gravis); trauma to the brain (head injuries, postoperative neurosurgical conditions, cerebral vascular accidents); respiratory depression (industrial poisons, suicide, overdosage of medicaments and anesthetics); and in ventilatory insufficiency following pulmonary resection. Many of these patients now die not of their primary lesions but from complications arising from decreased pulmonary ventilation.

Congenital Atresia of Esophagus. G. H. Humphreys, B. M. Hogg and J. Ferrer. J. Thoracic Surg. 32:332-346 (Sept.) 1956 [St. Louis].

This report deals with 136 cases of congenital esophageal atresia with and without fistula in infants seen at Babies Hospital or born in Sloane Hospital, both now units in the Columbia-Presbyterian Medical Center in New York, in the half century between 1903 and 1953. Over the last decade successful surgical treatment has been possible, and since then larger numbers of infants with this anomaly have been observed. The defect is not so infrequent as the earlier experience suggested; either it was unrecognized or little effort was made to treat it in the earlier period because of the apparent hopelessness of the situation. It is probable that the incidence, about 1 in 3,000 births, has not changed. The type of anomaly in this series was about the same as that described by others; in 122 of the 136 patients the esophagus ended in a blind pouch high in the posterior mediastinum and the lower segment originated in a fistula from the membranous portion of the trachea, the carina, or one of the primary bronchi. All but two of the recoveries occurred in this group. It seems probable that an incomplete cleavage between trachea and esophagus, together with failure of recanalization of the esophagus, will explain all the types of the anomaly. Of the total group of 136 patients, 75 are known to have had other congenital malformations. Among the 104 who died, 93 were examined at autopsy and 61 of these showed other anomalies; of the remaining 11 in whom autopsy was not performed, 5 showed gross associated anomalies. Thus, two-thirds of the infants who died were handicapped by other malformations. In contrast, among the 33 survivors only 9, or fewer than one-third, showed other anomalies.

Of the 101 patients operated on, 32 survived and 29 of these were living and well at the time of this study. Factors influencing survival are the size and degree of prematurity of the infant; the association with other severe malformations; the awareness of doctors and nurses caring for newborn infants of the possibility of the condition and their alertness in recognizing the characteristic symptoms; the promptness with which patients are referred for surgery; the care in preoperative and postoperative management; and the technical aspects of the operation itself. The first two factors are uncontrollable. The others give room for improvement. While occasional patients present anomalies that require multiple-stage procedures before swallowing can be restored, in the majority, successful end-to-end anastomosis of the esophagus is possible, with satisfactory restoration of normal swallowing.

Congenital Diaphragmatic Hernia and Hypoplastic Lung: A Clinical Evaluation. B. B. Roe and H. B. Stephens. J. Thoracic Surg. 32:279-290 (Sept.) 1956 [St. Louis].

A number of reports on congenital diaphragmatic hernia indicate that the condition can be surgically corrected with a low mortality rate, but the authors observed that the compressed and hypoplastic lung in the previously occupied pleural space could not be expanded after removal of the abdominal organs. They studied the hospital records and autopsy protocols of all cases of congenital diaphragmatic hernia in 11 San Francisco hospitals for as long as records were cataloged, up to 20 years. In all, 47 cases were analyzed for pregnancy factors, obstetric course, birth weight, presenting signs, time of operation, operative findings, length of survival, and autopsy observations. They found that the mortality rate in the newborn group was 87% as compared to 12% in the older patients (over 14 days of age), suggesting that natural selection plays an important role in the results. Surgical mortality was 67% in the newborn infants and 8% in the older group. Hypoplastic lung was an associated finding in nearly all patients that came to autopsy. Average combined lung weight was 44% of normal. The lung was found to be undeveloped on the side of the hernia in 10 of the infants who received surgical treatment and in 17 of those who came to autopsy (weight ratios of 0.13 to 0.91).

It is possible that clinical inexperience, technical difficulties, and other hazards of operating on the newborn infant are responsible for the high mortality rate. Surgical results are distinctly better despite these same disadvantages after two weeks of life and better respiratory compensation. The process of natural selection in the early neonatal period removes the patients with inadequate respiratory capacity. This period is also of positive value in improving the gradually acquired ventilatory capacity of an infant and rendering him a better surgical risk after a few days despite the hernial contents in the chest. Proponents of early surgical intervention argue that no harm is done by an unsuccessful attempt to help those whose unpredictable fate has already been sealed. They hope to salvage the borderline patient who might have an expansible lung and survive if the mechanical pressure were removed but who would not otherwise survive. The authors believe that more patients with marginal respiratory capacity at birth will survive if surgical intervention is delayed 10 days than if it is carried out immediately. Those with inadequate capacity will die whether they are operated on or not.

Hypophysectomy in the Treatment of Advanced Cancer of Breast. B. S. Ray and O. H. Pearson. Ann. Surg. 144:394-406 (Sept.) 1956 [Philadelphia].

Ray and Pearson discuss the benefits of hypophysectomy in the management of advanced mammary carcinoma in women. In the 22-month period between March, 1954, and December, 1955, 75 operations were performed on 74 women. Evaluation of the results is based on a follow-up of from 3 to 24 months. The operation employs a coronal scalp incision behind the hairline; opening of the right frontal bone; elevation of the right frontal cerebral lobe; division of the right olfactory nerve; division of the hypophysial stalk; enlargement of the opening in the diaphragm sellae; removal of the pituitary gland by curettement and suction followed by exposure of the sella turcica to Zenker's fluid; and closure of the wound without decompression.

There were seven deaths in the first 30 days after the operation, though only three could be attributed directly to the operation. Of the 67 patients who survived the operation, 36 had objective remission of their disease and 31 were not benefited. New remissions can be obtained by hypophysectomy in patients who derived temporary benefit from castration or from a combination of castration and adrenalectomy. Every patient who was temporarily benefited by castration obtained a new remission after hypophysectomy, and 4 of 11 patients who had had both castration and adrenalectomy obtained a new remission after hypophysectomy. It is suggested that if hypophysectomy is not employed as the initial ablative operation in altering endocrine influence on the disease, it is probably preferable to adrenalectomy as a second operation after castration. The survival period is more than twice as long in patients who obtain a remission after hypophysectomy as it is in those who do not, and the difference should be even greater when more time has elapsed.

Breast Cancer and Pregnancy: Report of 49 Cases Followed 5 Years. T. T. White and W. C. White. Ann. Surg. 144:384-393 (Sept.) 1956 [Philadelphia].

The authors collected 49 cases in which mammary cancer was associated with pregnancy from six hospitals in Seattle and from three hospitals in New York City. Of 11 patients treated for cancer of the breast while they were pregnant, 4 had lesions limited to the breast. Two of these four women died within a year, whereas two survived for 14 years, one still being free from cancer after this interval and the other dying from cancer in the opposite breast. All of the seven women who had involvement of the axillary lymph nodes died within four years. In 14 patients, the tumor was first noted during pregnancy and treatment was deferred until the nursing period. The average delay in treatment was 11 months. There were 3 such patients with disease localized to the breast and 11 in whom axillary nodes were involved. One of the three patients with localized disease survived seven and one-half years, while the other two survived three and one-half years at the end of which one was dead and the other was lost to follow-up. All of the 11 patients with axillary spread were dead in less than five years. The 12 patients with tumors found and treated during nursing appeared to have been treated more promptly than those in whom the tumor was first found in pregnancy. There was an average delay in treatment in this group of 3½ months and an average survival period of 52 months. Three of the 5 without axillary spread and 2 of the 7 with it in this group of 12 survived five years or more. Of the 12 patients operated on for breast cancer who later became pregnant, 7 survived 10 years or more, 2 of these for 34 years without recurrence. The interval between operation and subsequent pregnancy in all was four years or less.

The authors conclude that about one-third of the patients who develop breast cancer during the child-bearing period will have pregnancy as a complication during or after the occurrence of the cancer. Patients treated during pregnancy or nursing without spread of the disease beyond the breast have a prognosis similar to that which prevails in the absence of pregnancy or lactation. Patients with axillary spread of the cancer are usually in an advanced state of disease because of delay in treatment. The prognosis of patients who become pregnant after operation appears to be unusually good. Although abortion, spontaneous or induced, did occur in six patients, there was no evidence that it had produced any benefit.

Causes of Reintervention After Gastric Resection for Peptic Ulcer: A Contribution to the Study of the Complications in Stomach Operations. A. Medici and L. Contorni. Ateneo parmense 27:445-471 (May-June) 1956 (In Italian) [Parma, Italy].

The authors studied the causes for reintervention after gastric resection for peptic ulcer and the late complications that occur after operations on the stomach. All the cases treated in their institute in the last four years were critically reviewed. From January, 1952, to February, 1956, of a total of 2,828 surgical interventions, 457 were concerned with gastroduodenal pathology. Reintervention on the jejunal stoma was performed in 53 or 11.67% of all cases. In 43 cases reintervention was made necessary by lesions that occurred on the stomach or the duodenum or by some acute complication such as perforation. Only from 80 to 85% of the patients were well after the first operation. Postanastomotic peptic ulcer is the predominant chronic or late complication that calls for reintervention. Polyposis of the anastomotic stoma is a very rare lesion after gastroduodenal resection for peptic ulcer.

Bleeding Esophageal Varices: A Study of the Cause of the Associated "Hepatic Coma." W. V. McDermott Jr., J. Wareham and A. G. Riddell. Ann. Surg. 144:318-335 (Sept.) 1956 [Philadelphia].

In a group of 118 patients with portal hypertension who entered the hospital with massive gastrointestinal bleeding, 68 died. Only 18 of these 68 deaths were directly attributable to exsanguination, and 12 were due to causes not related to hepatic function. Thirty-eight of the patients who died in coma did so without manifesting either severe shock or uncontrollable and exsanguinating hemorrhage. This indicates that blood loss alone does not account for the high mortality. This paper is concerned with experimental and clinical studies designed to clarify the role of massive gastrointestinal hemorrhage in precipitating the so-called hepatic coma. Ten experiments were carried out on five healthy adult mongrel dogs in whom an Eck fistula had been constructed from 1 to 20 months before the experiments. Normal adult mongrel dogs on which three experiments were done were used as controls. The implications of these experiments on animals are discussed in connection with the results of clinical studies on 18 patients with bleeding esophageal varices and concomitant central nervous system symptoms who entered the Massachusetts General Hospital during the years from 1953 to 1955.

All of the patients studied showed striking elevations in the peripheral blood ammonia level, and the degree of elevation correlated well with the severity of the central nervous system symptoms. Some biochemical abnormalties associated with the introduction of blood into the gastrointestinal tract in the presence of spontaneous or surgically constructed portal-systemic shunts suggest that the syndrome of hepatic coma so commonly seen in patients with bleeding esophageal varices is due to ammonia intoxication. A program for the management of bleeding esophageal varices is outlined. Control of hemorrhage is of primary importance, because, even though there is no apparent threat of exsanguination, it is imperative to prevent the accumulation of a nitrogenous pool in the gastrointestinal tract. This may be accomplished initially by balloon tamponade and, when stabilization has been achieved by transfusions, by direct transthoracic ligation of the varices. Most of the blood can be removed by catharsis. Antibiotics should be given, because by depressing the bacterial count in the gastrointestinal tract the sources of urease and aminoacid oxidase can be controlled. L-glutamic acid has proved to be a valuable adjunct to therapy and may be given orally or parenterally in the glutamate form.

Wound Healing: A New Perspective with Particular Reference to Ascorbic Acid Deficiency. J. E. Dunphy, K. N. Udupa and L. C. Edwards. Ann. Surg. 144:304-317 (Sept.) 1956 [Philadelphia].

Experiments were conducted on 72 male guinea pigs weighing between 250 and 350 gm. Thirty-two animals were used as normal controls and 40 were placed on the standard scorbutogenic diet of Sherman for 20 days before wounding. The control animals were given a diet supplemented with vitamin C in the form of fresh vegetables and oranges. Wounding was done as follows: Under ether anesthesia the back of the animal was shaved and the skin prepared with a 2% isopropyl alcohol solution. Two circular wounds were made on the interscapular area of the back of each animal measuring about 3 cm. in diameter. The skin, subcutaneous tissue, and superficial muscles of the back were excised. Bleeding points, if any, were clamped and ligated with fine catgut. No dressings were applied. The wounds were allowed to heal without any further local treatment. On the 4th, 8th, 12th, and 16th days after wounding, the animals were killed by an overdose of ether anesthesia. One of the two wounds in each animal was utilized for histological and histochemical studies and the other for chemical analyses.

Chemical and histochemical studies provide a new perspective of wound healing based upon a "humoral" as well as a "cellular" approach. Significant differences in the pattern of healing in normal and depleted animals can be detected by these methods. In ascorbic-acid-deficiency fibroplasia, mucopolysaccharide production and the formation of reticular procollagen material are not inhibited and may be considerably increased. The basic defect of repair in ascorbic acid deficiency appears to be one of collagen synthesis. Evidence is presented to show that this defect is corrected within 24 hours after the intramuscular administration of ascorbic acid. A sponge biopsy technique that permits the study of repair by these methods in primarily closed wounds is described. Preliminary observations indicate that it can be applied effectively to a study of wound healing in man.

The Management of Inguinal Hernia in Infancy and Early Childhood. C. W. McLaughlin Jr. and C. Kleager. A. M. A. J. Dis. Child. 92:266-271 (Sept.) 1956 [Chicago].

The authors report observations on a consecutive series of 298 inguinal hernias seen in 240 infants and small children on the surgical service of Children's Memorial Hospital in Omaha. Inguinal hernia was the commonest congenital lesion for which infants and children were admitted to this hospital. Two hundred seventeen of the patients were males and 23 were females. In almost 60% of the children the hernia was noted before they completed their first year of life. Twenty-six infants were admitted with incarcerated hernia, but no strangulation of intestine was observed in an infant. This series of 298 hernias included 20 with associated hydroceles and 5 with hydroceles of the testis. Eleven patients in this group had undescended testes cared for at the time of herniorrhaphy. More than three-fourths of the complicated hernias in this series occurred in infants under 6 months of age. During the past 15 years the authors have recommended the immediate repair of all inguinal hernias regardless of age. While herniorrhaphy is a more difficult operation in a child under the age of 3 months than it is in older children, familiarity with the infant anatomy, the use of fine instruments, and, above all, delicate handling of tissues make it a sound surgical procedure.

Effect of Bilateral Adrenalectomy on Metastatic Choriocarcinoma from Teratoma of the Testis. N. S. R. Maluf, R. K. Loeffler and E. E. Erickson. J. Clin. Endocrinol. 16:1217-1226 (Sept.) 1956 [Springfield, Ill.].

Although it is plausible to consider that the growth of testicular tumors may be under hormonal control, there is no clear example of regression of a testicular tumor or of its metastases after orchiectomy or adrenalectomy except in patients also receiving radiotherapy. In the patient of this report, who had chorionic metastases from a teratoma of the testis, bilateral adrenalectomy produced no apparent benefit. Serial radiographs of his chest showed no change in the growth rate of measured discrete metastatic nodules.

NEUROLOGY & PSYCHIATRY

Prolonged Hypothermia in Treatment of Massive Cerebral Hemorrhage: A Preliminary Report. D. A. Howell, J. G. Stratford and J. Posnikoff. Canad. M. A. J. 75:388-394 (Sept. 1) 1956 [Toronto, Canada].

In massive cerebral hemorrhage death is generally caused by the tentorial pressure cone. The cerebral hemispheres increase in volume, and this swelling displaces the brain-stem downwards, producing ischemia of the posterior diencephalon, midbrain, and pons. Ischemic necrosis continues as long as the pressure remains high in the hematoma, and it usually proceeds more rapidly in patients with high blood pressure. The slower-developing cerebral hematomas in normotensive patients may be evacuated at craniotomy in the first few days of illness. The brain can be made slack and the hemispheres reduced in volume in three different ways: by dehydration, arterial hypotension, and hypothermia. Reducing the cerebral volume by hypothermia has distinct advantages. This was demonstrated in eight patients with massive intracranial hemorrhage. The patients were cooled by means of ice bags in the groins and axillae, alcohol sponging, and fans until the rectal temperature fell to between 32 and 30 C (90 and 86 F). Opening the windows during the Canadian winter hastened the fall in temperature, and once a patient was immersed for an hour in a bath to which ice was added. The patients were placed semiprone to prevent inhalation of vomit, and care was taken to prevent the upper shoulder from dropping forward and obstructing the venous return from the head. Tracheotomy was employed on several occasions to facilitate aspiration of secretions. Chlorpromazine, 50 mg., was given by intramuscular injection at the onset, and half this dose was repeated whenever the patient shivered or vomited.

Hypothermia influenced the course of the disease in every patient. Seven showed some improvement and two survived. Survival of two of eight patients with fulminating spontaneous intracranial hemorrhage is not an impressive result. However, in no case was prolonged hypothermia without influence. The progress of the pressure cone was arrested, and there was a dramatic improvement. Gastric hemorrhage was the most serious complication. It developed in four patients and possibly in a fifth either during the hypothermia or up to seven weeks after the onset of the illness. The authors attribute it to the small superficial ulcers secondary to brain damage of the type described by Cushing. Such ulcers were found at autopsy in two patients. This complication was unexpected, as gastric hemorrhage is not commonly seen in patients with cerebral hemorrhage. Death was averted in later cases by blood transfusions. One patient had a severe nosebleed most easily attributed to hypertension, and another was found, at autopsy, to have an adrenal hemorrhage. Mild uremia developed in all patients, and anuria in three. Pneumonia was a serious complication in three patients. Aseptic venous necrosis developed in two patients, possibly as the result of the negative water balance. Weeping eczema of the scrotum was seen in one patient, possibly caused by prolonged contact with ice bags. Various auricular arrhythmias were transient and harmless. Prolonged hypothermia is a powerful method of reducing the cerebral volume and thereby relieving the acute tentorial pressure cone.

Hereditary Pellagra-like Skin Rash with Temporary Cerebellar Ataxia, Constant Renal Amino-Aciduria, and Other Bizarre Biochemical Features. D. N. Baron, C. E. Dent, H. Harris and others. Lancet 2:421-428 (Sept. 1) 1956 [London, England].

Preliminary studies are reported on a new syndrome that began in 1951 when a boy was hospitalized who apparently had severe pellagra associated with a neurological disorder. His urine contained a consistently large amount of amino acids. This led to many further biochemical investigations, and it soon became apparent that he had a bizarre and hitherto undescribed syndrome. Studies of the boy's relations revealed similar biochemical features in three of his seven siblings, one of whom had been admitted several years previously to the Middlesex Hospital with a similar pellagra-like syndrome. The eight siblings were the offspring of a first-cousin marriage. The most constant clinical feature of this new disease, which has been referred to as Hart's syndrome, or now preferably as "H" disease, is a tendency to develop a rough reddened skin on exposure to moderate sunlight. In two of the siblings, greater exposure led on more than one occasion to a severe rash that appeared identical with that of pellagra. On occasion a severe but fully reversible cerebellar ataxia developed in association with the rash and also (in one of the patients) following infective disease without rash. The older affected siblings are also mentally retarded.

Among the biochemical findings is a constant gross renal aminoaciduria of unique pattern, without other evidence of renal dysfunction. This is the most specific abnormality by which the disease can be identified. There is also a constant large excretion in the urine of indole-3-acetic acid and a less constant large excretion of indican. The feces contain a moderately increased quantity of protoporphyrin. The authors wonder if the immediate biochemical disorder producing the clinical syndrome is an abnormality of nicotinic-acid utilization. In recent years a number of new clinical syndromes have been described in association with gross metabolic disorders. The biochemical disorder usually helps to diagnose the disease since it may be more constant and characteristic than are any of the clinical features. This latter point especially applies to hereditary diseases, where the action of a gene may show itself by a constant gross biochemical abnormality even when the clinical signs remain ambiguous and fluctuate in intensity.

A Psychotherapeutic Technique with Large Groups in the Treatment of Alcoholics: A Preliminary Report. J. J. Armstrong and R. J. Gibbins. Quart. J. Stud. Alcohol 17:461-478 (Sept.) 1956 [New Haven, Conn.].

The authors found that in the early stages of treatment alcoholic patients frequently remain anxious and easily disturbed, with many defenses against obtaining much-needed insight through formal psychotherapeutic interviews. Many alcoholic patients present personality problems that involve difficulties in their dealings with authority. The group setting, however, is often comparable to aspects of a society the patient is used to, in that it is composed of people with similar attitudes, interests, and abilities, but not drinking at the moment. An attempt was made to establish a group with some homogeneity. Originally, the only patients accepted for the group were those who were undergoing or had undergone individual psychotherapy or at least a psychiatric evaluation. Soon patients were directed to the group right from the intake conference. The weekly attendance gradually rose to an average of 35, which prevailed during the period of the present study. Of 32 persons who attended at least 15 sessions, 23 improved, 7 could not be traced, and 2 received no help. The conclusion was reached that the group method of treatment for alcoholics provides certain distinct advantages over individual therapy by lessening the patient's need to reject authority as symbolized by the therapist, reducing anxiety engendered by transference situations, allowing a more permissive setting than rigidly scheduled individual interviews, and permitting a sharing of experiences toward a common goal with others having comparable problems.

Intraspinal Epidermoid Tumours (Cholesteatomas) in Patients Treated for Tuberculous Meningitis. C. Choremis, D. Economos, C. Papadatos and A. Gargoulas. Lancet 2:437-439 (Sept. 1) 1956 [London, England].

Dermoid and epidermoid tumors in the central nervous system are variously called pearly tumors, epidermoid teratomas, dermoid endotheliomas, and cholesteatomas. The usual sites of these tumors are the lumbosacral spinal canal, the middle ear, the vicinity of the pituitary gland, and between the tables of the skull. At the Children's Clinic of the University of Athens the authors recently had occasion to study five children, ranging in age from 7 to 12 years, who had pearly tumors in the thoracolumbar spinal canal. All these children had been successfully treated from three to seven years earlier for tuberculous meningitis. The authors believe that the two conditions are closely related. They think that repeated lumbar punctures in the course of streptomycin therapy may implant epithelial cells which in time form these tumors. They hope that this report will alert physicians to the recognition of a curable condition arising as a complication of the treatment of tuberculous meningitis.

The Pathological Effects of Cerebral Arteriography. T. Crawford. J. Neurol., Neurosurg. & Psychiat. 19:217-221 (Aug.) 1956 [London, England].

Cerebral arteriography is usually without harmful effects; nevertheless, there is inevitably some damage to the arterial wall, and in a very small proportion of cases harmful effects ensue. Crawford reports observations on autopsy material from 75 subjects on whom arteriography had been carried out at intervals varying from two hours to eight months before death. This material came from many different sources and was not confined to the autopsies from a single neurosurgical unit. The most serious ill effects observed were carotid thrombosis and cerebral embolism. It was not possible to assess the frequency of these rare misfortunes. They are more liable to occur in elderly hypertensive arteriosclerotic patients.

Infantile Encephalomalacia with Multiple Cavity Formation. B. J. Alpers, R. A. Farmer and H. E. Yaskin. A. M. A. Arch. Neurol. & Psychiat. 76:229-235 (Sept.) 1956 [Chicago].

The authors report on studies on the brain of a boy who died at the age of 3½ months and in whom encephalomalacia with multiple cavity formation was discovered. The mother was in good health during pregnancy but one week before delivery had an attack of pneumonia. There were no seizures at birth. At 2 weeks of age the infant developed "growling respiration," and at 7 weeks he had a bloody nasal discharge, extending his arms stiffly, and had a staring gaze. At 11 weeks he had attacks of cyanosis, in which he was found to twitch, stiffen out, and clench his fists. He had a generalized convulsion at 14 weeks. Examination at this time revealed that the child was unconscious, with hyperpnea, bilateral papilledema, retinal and subhyaloid hemorrhages, and generalized hyporeflexia. The spinal fluid and subdural fluid were grossly bloody. He had an erythrocyte count of 2,700,000 and 41,000 leukocytes per cubic millimeter, with lymphocytes predominating. He died within a few hours after his seizures.

Numerous cystic areas were found in both gray and white matter of the brain and in the basal ganglia regions, sparing brain stem and cerebellum. Microscopic study revealed pia-arachnoid thickening, profuse gitter-cell accumulation with cyst formation, often focal gitter-cell collections, calcium deposits in some of the areas of necrosis, and areas of only partial destruction of tissue. The blood vessels were on the whole intact, but endothelial swelling was present in some regions and many perivascular spaces were filled with macrophages and mononuclear cells. The features recorded in this case correspond well with those previously reported. Variations in the location and extent of the lesions have been observed from case to case. The outstanding variation in the present case consisted in extensive involvement of both the gray and the white matter. The pathogenesis of the encephalomalacia is not clear.

A Controlled Clinical Study of Chlorpromazine and Reserpine in Chronic Schizophrenia. M. Shepherd and D. C. Watt. J. Neurol., Neurosurg. & Psychiat. 19:232-235 (Aug.) 1956 [London, England].

Shepherd and Watt tried to assess the relative merits of chlorpromazine and reserpine. Twenty-four of the most deteriorated and apathetic female schizophrenic patients in a county mental hospital were chosen. Their ages ranged from 27 to 52 years. The length of stay in hospital varied from 7 to 29 years. Most patients were totally unoccupied, withdrawn, and unsociable. They took no interest in their appearance or personal care and were incontinent of urine. Talk was so seriously disordered that an intelligible conversation was impossible. Many patients were mute; a few were noisy, interfering, hostile, or destructive to clothing and property. The 24 patients were divided into three groups of eight by random selection. The experiment lasted 18 weeks, during which each group of patients received each of three substances—reserpine, chlorpromazine, and placebo, in different orders of administration. Chlorpromazine was responsible for improvement in a significantly higher proportion of cases than reserpine, and, in the doses employed, reserpine was responsible for the great majority of toxic effects observed. No satisfactory explanation for these differences can be offered because of the obscurity attending the mode of action of reserpine. It may be significant that the schizophrenic patients in the present study were chosen not for their aggressiveness and overactivity, as in most of the other studies cited, but because of their apathy and inertia.

Pyridoxine (Vitamin B_6) in Alcoholism. G. W. Atkinson and W. C. Kappes Jr. Virginia M. Month. 83:391-393 (Sept.) 1956 [Richmond, Va.].

Observations were made on 70 unselected patients with alcoholic intoxication. Thirty-five of these patients were given 500 mg. of pyridoxine hydrochloride (vitamin B_6) twice a day, whereas the other 35 served as controls, receiving only the treatment given to all of them. There was no significant difference in the recovery rate of those treated with pyridoxine and in the controls. The excretion rate of the alcohol was not altered by the pyridoxine, and no beneficial effect or change was observed after its use in alcoholic patients who had psychoses and convulsions. Although pyridoxine has been advocated by a number of observers for the treatment of alcoholic intoxication in human subjects, in experiments on mice it has proved ineffective or even dangerous in large doses.

Pseudotumor Cerebri: Benign Intracranial Hypertension. L. M. Davidoff. Neurology 6:605-615 (Sept.) 1956 [Minneapolis].

The author reports on 61 patients between the ages of less than 5 and more than 50 years with "pseudotumor" or benign intracranial hypertension, all of whom had true papilledema. Most of them complained of headache, and many of them had failing vision. All but one had a normal ventricular system as revealed by pneumoencephalography (either ventriculography or lumbar encephalography). The cerebrospinal fluid was under increased pressure but otherwise within normal limits as far as cell count and protein were concerned. Many of the patients complained of diplopia, and these usually showed interference with one or both sixth cranial nerves. In four male and five female patients symptoms developed after otitis media. In 11 male and 12 female patients symptoms developed after infections in the body elsewhere than in the ears or mastoids, or after a head trauma. The last group of 29 patients, 18 of whom were women, gave no history of preceding infection. The peak of the incidence in this group was in the fourth decade of life. Unusual obesity was noted in 3 of the 18 women.

The causation of this condition is still unknown and is probably variable. Patients in whom symptoms are preceded by infection of an ear or mastoid may well have mural thrombi in the superior longitudinal sinus or the major lateral sinus extensive enough to interfere with cerebrospinal fluid absorption. To some extent this may also be true of patients with preceding infection elsewhere than in the ear or mastoid, or with cerebral trauma. In the group of 29 patients in which the syndrome occurred more frequently in women and was more common in the middle decades of life, the condition may have been of a toxic or allergic nature, and in the women it may have been related in some manner to menstrual disturbances of electrolyte balance. Subtemporal decompression was performed in 51 patients and suboccipital decompression in one. In nine patients treatment consisted of dehydration measures and repeated lumbar puncture, after which they were placed on a salt-poor diet; fluid intake was limited, and ammonium chloride or Diamox was administered. The patients were followed up for from one to 22 years. Most of them recovered, but five had complications, which consisted of convulsive seizures in two, a tense decompression and blurring of the disk margins in one, subdural hematoma in one, and a slight degree of diencephalic dysfunction and a somewhat greater degree of focal abnormality at the site of the decompression in one. The prognosis in most patients is excellent, although many months or even several years may be required for the syndrome to subside completely. Because of the favorable outcome in most patients and the uncertainty as to the causation of the syndrome, the term "benign intracranial hypertension," suggested by Foley, especially for those cases not preceded by infection or trauma, seems a desirable one.

Course of Exacerbations of Multiple Sclerosis in Hospitalized Patients. J. F. Kurtzke. A. M. A. Arch. Neurol. & Psychiat. 76:175-184 (Aug.) 1956 [Chicago].

At the Bronx Veterans Administration hospital over 300 patients with a diagnosis of multiple sclerosis were hospitalized between 1944 and 1953, but in some of these the data for diagnosis were insufficient. This paper is concerned with the 220 patients in whom the diagnosis was definite. These patients were divided into two groups. Group A consisted of 175 patients whose present episode was of two years' duration or less before hospitalization. Group B was composed of 45 patients the duration of whose present exacerbation exceeded two years before admission and averaged four and one-half years. No patient improved whose present exacerbation had persisted for more than two years before admission. Of the 175 patients in whom the present episode had lasted less than two years, 33% improved, 50% had no change, and 17% became worse during a mean hospital stay of three and a half months. Thus one out of three patients improved while in the hospital with an episode that had persisted for less than two years before admission. Follow-up studies after hospitalization in one-third of this group revealed only three patients who improved later but who had not improved in the hospital. It was felt that the period of hospitalization, which averaged three and a half months, was sufficient for the investigation of possible prognostic features. The outcome of the present episode could not be correlated with the total duration of illness, the age on admission or onset, the type of neurological involvement, the severity of status on admission, the prior nature of the illness, the laboratory findings, the month or year of admission, or the month of onset of acute attacks.

Improvement or remission was inversely related to the duration of the episode before admission. Of the 28 patients in whom the present episode had existed less than 7 days before admission, 24 improved, 2 remained unchanged, and 2 became worse; of the 14 in whom the present episode had existed between 8 and 14 days, 9 improved and 5 remained unchanged; of the 26 in whom the episode had existed for from 15 to 31 days, 10 improved, 14 remained unchanged, and 2 became worse; of the 75 in whom the episode had existed for from 1 to 12 months, 12 improved, 45 remained unchanged, and 18 became worse; and of the 29 in whom the episode had lasted between one and two years, 2 improved, 22 remained unchanged, and 5 became worse. This relationship of improvement to the duration of the episode may provide a standard for comparison and prognosis in this disease.

GYNECOLOGY & OBSTETRICS

Neonatal Umbilicus as a Source of Streptococcal Infections in a Maternity Unit. J. M. Boissard and B. Eton. Brit. M. J. 2:574-576 (Sept. 8) 1956 [London, England].

Pyrexia developed suddenly in a puerperal woman six days after an uneventful delivery. Mother and infant were removed to the isolation ward. Culture of the mother's vaginal swab yielded a heavy growth of Streptococcus pyogenes type 9. Nose and throat swabs were cultured from the ward staff and vaginal, nose, and throat swabs from all patients. None showed Str. pyogenes. A midwife, who had been working on the ward for only a week, went on leave two days before pyrexia developed in the puerperal woman. Acute tonsillitis, later shown to be due to Str. pyogenes type 9, developed in the midwife while she was at home, on the same day the puerperal woman had shown pyrexia. The infections in the mother and midwife manifesting themselves on the same day suggested a common source rather than one that was derived from one or the other, and the findings in the infant (cultures from throat and umbilical cord yielding Str. pyogenes type 9) prompted investigation of the nursery from this point of view. Cultures of swabs of the umbilicus of four infants who had been discharged from the nursery yielded Str. pyogenes type 9. Although these infants were widely dispersed at the time of this investigation, it seems certain that they acquired their umbilical infection in the ward nursery—the one environment originally common to all.

The authors show that the infections in the adults were accidents in what was primarily a series of infections in infants. There was never a time from the beginning of the earliest-known infection until the closure of the ward when the nursery was free from infection. Nothing is known about how or when infection entered the nursery, but it seems reasonable to suppose that the most likely route was via an attendant who was in the early stages of an unrecognized infection. The outbreak demonstrates the following points: 1. In a maternity hospital the nursery was the source of infections due to Str. pyogenes. 2. Without investigating the nursery it would have been impossible to find a connecting link between the infected adults or to detect the source of their infection. 3. If the nursery had not been investigated, it might not have been possible to control the outbreak of streptococcic infections. The authors make a plea for bacteriological investigation of the nursery whenever a case of streptococcic infection is found in a mother or a member of the staff.

The Combination of Prednisone and Methylandrostendiol in the Treatment of Advanced Cancer of the Uterus. G. Pescetto. Minerva ginec. 8:552-556 (July 15) 1956 (In Italian) [Turin, Italy].

Fourteen patients with cancer of the uterus in an advanced stage were treated with a combination of prednisone and methylandrostendiol. The author divided the patients into three groups. To the first group belonged six patients with uterine cancer located in the portio or in the body of the uterus. Surgical intervention had to be excluded because of the advanced stage of the disease. These patients were subjected to roentgenotherapy for a minimum of 9,000 r and a maximum of 12,000 r. Five of the six patients could no longer tolerate irradiation. To the second group belonged five patients with relapse of cancer of the uterus. These patients had received from 9,000 to 12,000 r. Severe pain was present. To the third group belonged three patients with cancer of the portio who received radium and roentgenotherapy. Marked cachexia and severe pain were present.

The dose of the combination was 100 to 150 mg. of prednisone and 100 to 150 mg. of methylandrostendiol, depending upon the condition of the patient. Treatment lasted 20 days, and in five patients it was started again after a 10-day interval. For the first five or six days after the treatment, 10 to 15 mg. of prednisone per day was given. Pain was markedly relieved in 80% of the patients, and in the others it was diminished. The general and psychic condition of the patients improved. The combination of the two drugs protected the patients against x-ray sickness. The negative aspect of the treatment lies in the short duration of the results, the lack of any evident effect of the drugs on the neoplasia, and the very high expense involved.

Cancer of the Cervix, an Appraisal. J. V. Meigs. Am. J. Obst. & Gynec. 72:467-478 (Sept.) 1956 [St. Louis].

Meigs reviews the results obtained in 130 patients with cervical cancer in whom he personally performed the operation. The following patients survived five years: Of 61 who received surgical treatment only, 55 (90%); of 29 who were subjected to surgery after radiation had failed, 18 (62%); of 20 who were operated on after cure had been achieved by irradiation (no cancer found at operation) 19 (95%); of 10 in whom surgery was followed by postoperative irradiation (surgical failures), 3 (30%); and of 10 who received irradiation before and after surgery (radiation and surgical failures), one (10%). The 10-year survival rates indicate that those treated by surgery alone obtained results that were as favorable as those treated by irradiation plus surgery, but it should be remembered that the patients operated upon were probably the best-risk patients. It is conceivable that surgery will cure some radiation failures and that radiation will cure some of the surgical failures. This definitely indicates the importance of selection. The author hopes that study of the sensitization response and of the radiation reaction will help in the work of selection. The cure of patients in whom the lymph nodes have been invaded is excellent, running from 31 to 55% in the five-year results and to from 25 to 40% in the 10-year results. Radiation therapy seems to be as effective in patients with as without invasion of the lymph nodes. This study suggests that radiation and surgery are complementary and that results in the hands of experts will be good whichever method is used, but it does show the importance of selection.

The Pregnant Diabetic: A Report of 200 Cases. S. G. Clayton. J. Obst. & Gynæc. Brit. Emp. 63:532-541 (Aug.) 1956 [London, England].

This report is based on the records of 201 pregnancies in 176 diabetic patients. Although delivery was carried out by cesarian section in 122 patients and by abdominal hysterectomy in 6, and delivery was induced in most of the others, there was only one maternal death. This low maternal death rate, however, does not imply that there is no risk; on the contrary, the risk is great in those in whom albuminuria occurs during the early months of pregnancy, in those with retinal hemorrhages, and in those with hypertension. These patients may not all have the same pathological changes, but many probably have glomerulosclerosis (Kimmelstiel-Wilson syndrome). The fetal mortality remains high when pregnancy is complicated by diabetes. The three multiple pregnancies (two twin and one triplet pregnancy) produced only two living infants. In the 198 pregnancies with single fetuses only 132 infants remained alive; the pregnancy was terminated in 8 cases, spontaneous abortion occurred in 7, stillbirth in 21, and neonatal death in 30. The weight of the infants of diabetic mothers is often excessive, but the overgrowth of the placenta is even more pronounced, being about 25% instead of the normal 17% of the fetal weight at 36 weeks of pregnancy. Hydramnios occurred in 48% of the single-fetus pregnancies.

If diabetic pregnant women are permitted to go to full term, the fetus not infrequently dies in utero during the last four weeks of pregnancy. On the other hand, if the infant is delivered prematurely, there is a considerable risk of neonatal death. The relative frequency of these two modes of death will depend on the obstetric management, and since most of these women were delivered at about the 36th week the stillbirth rate in this series is relatively low. All the intrauterine deaths recorded here occurred between the 32nd and 36th weeks of pregnancy, and, because of the author's policy of delivery at about the 36th week, the risk of intrauterine death after that time could not be ascertained. If control of the diabetes is poor, the number of intrauterine deaths is increased, but even with good control not all these deaths will be prevented. The neonatal deaths occurred most frequently after cesarian section, probably because that was the commonest mode of delivery (122 cases). The child is delivered together with the usual flood of amniotic liquor. Often large quantities of fluid are aspirated from the air passages and from the stomach. All goes well for a time, but after a few hours respiratory distress begins, with successive cyanotic attacks until circulatory failure occurs. This mode of death was seen in 23 of 30 cases, and in all those in which an autopsy was performed absorption atelectasis resulting from hyaline membrane formation in the air passages was found. The average time from birth to death was 13 hours.

A Comparative Study of Different Techniques for the Diagnosis of Cervical Carcinoma. H. E. Nieburgs. Am. J. Obst. & Gynec. 72:511-515 (Sept.) 1956 [St. Louis].

Not only racial, social, and age factors but also the techniques employed help to explain the conflicting reports on the number of cases of cervical carcinoma detected by exfoliative cytology. Three techniques were compared in 154 patients, including 73 women with different epithelial lesions of the cervix. A cotton applicator was used to prepare a smear from the posterior fornix. The endocervical smear was obtained by insertion of the cotton applicator into the cervical canal and twirling it around a few times against the squamocolumnar junction. The smear was made by rolling the cotton applicator in the counterclockwise direction on the slide in order to secure complete transfer of the cervical mucus plug to the glass. The third technique employed was the use of Ayre's wooden spatula for the scraping of the cervix without prior removal of the mucus plug. The smear from the posterior fornix was less satisfactory than those obtained from the endocervix. The occurrence of false-negative smears obtained from the endocervix seems to depend on the order in which the smears are taken. The first smear made appears to be the more satisfactory, apparently because of the fact that the endocervical mucus plug, which usually carries a larger number of cancer cells, was utilized. Smears obtained with the cotton applicator or spatula following the removal of the mucus plug may result in false-negative slides. Although in positive cases the spatula smears contain a larger number of cells, for routine cancer detection less time seems to be required for the interpretation of slides when the cotton applicator smears are used.

Pelvic Carcinoma Following Irradiation for Benign Gynecological Diseases. J. P. Palmer and D. W. Spratt. Am. J. Obst. & Gynec. 72:497-505 (Sept.) 1956 [St. Louis].

The authors first studied the records of 377 women with cancer of the body of the uterus seen at the department of gynecology of Rosewell Park Memorial Institute between 1947 and 1952. They found that 21 patients had had previous irradiation of the pelvis, 17 for benign uterine conditions and 4 for nonuterine pelvic cancer. The average interval between the irradiation and the subsequent corpus cancer was 11.7 years. At Rosewell Park Memorial Institute, before 1940, the treatment of benign uterine conditions with radium or x-ray or both was common practice. Since 1940, irradiation for benign bleeding has been given only if surgery was contraindicated. This change of policy came with the realization that occasionally a patient who had had irradiation for benign bleeding would return with uterine or other pelvic cancer. Realizing the long intervals elapsing between irradiation and the development of cancer, the authors considered in their further investigations only patients treated prior to 1941. Questionnaires were mailed to 1,670 patients who had been treated between 1930 and 1940 with radium and/or x-ray for benign uterine abnormalities. The women were asked (1) their opinion as to whether the symptoms were relieved, (2) Whether these symptoms later recurred, and (3) Whether any pelvic operation or irradiation was subsequently necessary. If question 3 was answered "yes," the doctor and/or hospital was then asked for full data. Adequate replies were received from 721 patients. All of these patients were followed for 12 or more years; the average follow-up was 16.08 years. It was found that pelvic cancers had developed in 61 or 8.4% of the 721 patients. The authors also cite figures on the expected incidence of cancer, comment on the role of fibroids and endometrial hyperplasia in the causation of cancer of the body of the uterus, and compare radiation dosages.

They conclude that their detection of a higher incidence of pelvic cancer developing after irradiation can be explained by the fact that the follow-up of other investigators was not long enough. They found a rather low incidence of menorrhagia of the menopause in patients with cancer of the body of the uterus, and they deduce from this that menorrhagia, or its underlying cause, is not a significant predisposing influence in the development of subsequent malignancy of the corpus uteri. They believe that the previous irradiation is, at least in part, responsible for the subsequent cancers. Also, since the patients with controlled cancer of the cervix did not show the high incidence of subsequent cancer of the adjacent pelvic structures, they believe that the relatively low irradiation dosage given the group with benign lesions caused some growth-stimulating influence that the higher, cancerocidal dosage did not cause. Irradiation castration should be used only in women who are not satisfactory surgical risks and, if used, should probably be given in dosage adequate to overcome the possible growth-stimulating influence. The authors continued their studies after they wrote this report, and in an addendum they add 25 patients to the 721 originally studied. They also add 10 pelvic cancers to the 61 mentioned in the paper. The shortest interval between irradiation and cancer development was 13 years and the longest 23 years; the average was 17.3 years.

The Outcome of Pregnancy Complicated by Threatened Abortion. E. P. N. Turnbull and J. Walker, J. Obst. & Gynæc. Brit. Emp. 63:553-559 (Aug.) 1956 [London, England].

It is generally considered that if bleeding ceases and a pregnancy complicated by threatened abortion continues, the end-result will be good, but the observation that the hemoglobin and red blood cell levels in the baby's cord blood at birth were higher than normal when there was a history of threatened abortion suggested that the oxygen supply of these fetuses had been abnormal. The authors present data on oxygen and hemoglobin levels and red blood cell counts in the cord blood of the fetus from pregnancies complicated by threatened abortion. A study of the outcome of pregnancy in cases of threatened abortion in Aberdeen Hospital cases indicates that the danger to the fetus is not over when the bleeding ceases. Of 155 women leaving hospital after apparently successful treatment of threatened abortion, 19% subsequently aborted. For those delivered after the 28th week, the prematurity, obstetric death, and antepartum hemorrhage rates were approximately three times as great as the average for all booked patients and the incidence of fetal abnormality about twice as great. The excessive fetal death rate was associated especially with prematurity and antepartum hemorrhage. The high proportion of very small babies was explained largely by the high incidence of premature labor, but there was also a suggestion that fetal growth was slightly depressed after threatened abortion. Neither the raised incidence of fetal abnormalties nor the type thereof was clearly related to the time of onset of bleeding. It is difficult to say whether these findings can be explained by a persisting or recurrent maternal defect that caused first threatened abortion and later antepartum hemorrhage and premature labor or whether damage to the deciduoplacental site at the time of the initial bleeding was itself sufficient to cause permanent impairment of function. Possibly either or both mechanisms may be present in any given case.

PEDIATRICS

Freeze-Dried B. C. G. Vaccination of Newborn Infants with a British Vaccine. M. I. Griffiths and W. Gaisford. Brit. M. J. 2:565-568 (Sept. 8) 1956 [London, England].

The Danish BCG vaccine has proved uniformly satisfactory for use in appropriate dosage in newborn infants. It suffers, however, from the defects inherent in any living liquid vaccine and it produces complications of a minor, but nevertheless undesirable, nature in a small proportion of cases. An efficient dried vaccine would offer so many advantages over a liquid preparation that it would become the standard form for universal use. The difficulties encountered in the preparation of freeze-dried vaccines have been in conserving an adequate number of viable organisms that will remain viable and in reconstituting the dried mass to produce a uniform suspension with minimal clumping. For the past 18 months the authors have been using a freeze-dried vaccine prepared by the method described by Ungar, Farmer, and Muggleton. They have vaccinated 1,100 newborn infants with various batches of this vaccine. A batch containing approximately 10,000 viable bacilli per inoculating dose was soon found to be antigenically inadequate and was discontinued. Another batch containing approximately 1 million viable organisms per inoculating dose was slightly more potent than the Danish liquid BCG in allergy production, but as it produced large lesions at the site of inoculation and glandular complications (5% of enlarged axillary nodes and 0.6% of nodal abscess formation) the authors consider that it is a little too potent for routine use. Two other batches containing 110,000-130,000 viable organisms per inoculating dose, although only very slightly less antigenic than the Danish vaccine, have produced no complications to date and appear to provide the optimal dose.

Agammaglobulinemia in Two Brothers. J. Haarstad. Acta med. scandinav. 155:125-129 (No. 2) 1956 (In English) [Stockholm, Sweden].

The author describes a typical case of agammaglobulinemia in two brothers. The two patients, aged 9 and 4 years, the only children of parents with normal serum gamma globulin levels as revealed by paper electrophoresis, had been ill almost all their lives. Both had a history of abnormal susceptibility to infections, recurrent periods of rises in temperature without apparent cause, pulmonary symptoms, dystrophy, slight increase in weight, thin and slimy feces, and delayed static motor development. The absence of gamma globulins in the patients' serums was revealed by electrophoresis. The older boy was admitted to hospital for the treatment of an acute attack of pneumonia that responded to the administration of streptomycin and penicillin; these drugs, however, had no effect when used for prophylactic treatment. The effect of treatment with 0.1 gm. of gamma globulin per kilogram of body weight was uncertain in the older patient, but weekly injections of the same dose of gamma globulin had a good prophylactic effect in the younger patient.

Hibernation in Poliomyelitis. F. C. Matera, A. R. Alvarez, B. Mesz and others. Arch. argent. pediat. 27:58-64 (Jan.-Feb.) 1956 (In Spanish) [Buenos Aires, Argentina].

Forty patients from 3 months to 14 years of age with poliomyelitis were treated by hibernation with the aid of chlorpromazine and promethazine. The patients were acutely ill with encephalitis, bulboencephalitis, bulboencephalospinal and ascending paralysis, and with intractable fever and severe metabolic disorders. They were given 1 mg. of chlorpromazine per kilogram of body weight intramuscularly one hour before the start of the treatment, as a test for sensitivity. Children below 3 years of age were given the drug intramuscularly in total daily doses of between 3 and 25 mg. per kilogram of body weight. The solution for intramuscular injection contained equal parts of the drug in the daily dose to be given plus 20 units of hyaluronidase for each cubic centimeter of the solution. The injections were given at intervals of 3 or 4 hours during the critical period, after which the intervals varied from 8 to 12 hours. Children between 3 and 14 years of age were given the drug intravenously in daily doses that varied between 2 and 8 mg. per kilogram of body weight. The total daily dose was prepared in a 5% dextrose solution and was given by infusion at an extremely slow rate. Warming of the patients (dehibernation) was started as soon as the acute symptoms were controlled. During this period the patient was given androgens, ascorbic acid, and corticoadrenal preparations. The symptoms rarely reappeared after the warming of the patient was started, but if they did the treatment was repeated. Simultaneously with hibernation, the patients were treated for their clinical condition. Hibernation reached a low degree in all patients, although large doses of the drugs had to be used at times. Duration of hibernation varied from four to nine days. Fever was lowered in 32 of the 40 patients. Five of the eight patients in whom fever persisted died. The treatment gave satisfactory results in 28 patients. In all, 12 patients died: 5 of the 8 with intractable fever, 3 out of the 15 who had tracheotomy, 3 out of 6 with edema, and one who died from respiratory paralysis during intravenous administration of the hibernating drugs. The authors conclude that hibernation has a sedative, hypnotic, hypothermic, and muscle-relaxing action by means of which the cellular metabolism is improved, the progression of specific lesions is prevented, and the reversibility of the lesions is assisted. This is a preliminary report.

A Distinctive Type of Biliary Cirrhosis of the Liver Associated with Cystic Fibrosis of the Pancreas: Recognition Through Signs of Portal Hypertension. P. A. di Sant'Agnese and W. A. Blanc. Pediatrics 18:387-409 (Sept.) 1956 [Springfield, Ill.].

Four boys and three girls between the ages of 4 and 10 years with cystic fibrosis of the pancreas and clinically manifest cirrhosis of the liver were studied. All seven had pulmonary disease characterized by generalized obstructive emphysema and chronic bronchopneumonia in varying degrees of severity. The increase in concentration of chloride and sodium in the sweat, characteristic of patients with cystic fibrosis, was present in all. Five patients had pancreatic deficiency as shown by the absence of trypsin in the duodenal contents. Tryptic activity and viscosity of the duodenal contents were low in the two remaining patients. Hepatosplenomegaly was present in all patients, but none had jaundice. The lack of consistency in the results of so-called liver-function tests was notable, since in some of the patients they were normal even when the hepatic process, especially the portal hypertension, was quite advanced. Biopsy of the liver in five patients, obtained at laparotomy, revealed cirrhosis. In four of these the venous pressure in the portal system was found to be markedly elevated, and surgical shunting procedures were performed to relieve the increased tension. Liver biopsy was not performed in two patients, but all seven presented clinical evidence of portal hypertension, although the symptoms of hypersplenism, gastrointestinal bleeding, or ascites were much more severe in the five patients who were operated on. Two of the children died of progressive pulmonary disease and a third from uncontrollable gastrointestinal hemorrhage. Four patients are alive; one of these had no recurrence of gastrointestinal bleeding within three years after splenectomy and a splenorenal vein shunt, but her pulmonary status had deteriorated; one patient was doing well after a portacaval shunt; in one patient the liver involvement was less serious than the pulmonary condition, and one patient was doing well but hypersplenism had recently appeared.

The name multilobar biliary cirrhosis with concretions was given to the advanced hepatic process observed in these patients, to emphasize the distinctive character of the cirrhosis in cystic fibrosis of the pancreas. Stress is laid on the fact that symptoms appear only when portal hypertension develops, leading to ascites, hypersplenism, or gastrointestinal bleeding. In only 7 of the 325 patients with cystic fibrosis of the pancreas who were seen at the Babies' Hospital in New York between 1935 and 1955 did the disease progress to this syndrome. While the total number affected by this condition, therefore, is not large, a survey of the diagnostic files shows that it accounts in this hospital for one-third of the pediatric patients with cirrhosis of the liver from all causes and for a much greater proportion of the children with portal hypertension secondary to hepatic fibrosis. An operative shunting procedure may be needed, as gastrointestinal bleeding may be the greatest immediate risk to the patient. The hepatic area thus must be added to the ones frequently involved in cystic fibrosis of the pancreas, and this disease must be included among the important causes of portal hypertension secondary to cirrhosis of the liver in children.

Patent Ductus Arteriosus with Reversal of Flow: Clinical Study of Ten Children. R. C. Anderson, P. Adams Jr. and R. L. Varco. Pediatrics 18:410-423 (Sept.) 1956 [Springfield, Ill.].

Eight girls and two boys between the ages of 16 months and 15 years with patent ductus arteriosus with reversal of flow (pulmonary artery to aorta) are reported on. Cyanosis of the nailbeds, often greater in the toes, was present in all. Exertional dyspnea occurred early. Murmurs were of no diagnostic value, but an accentuated pulmonic second sound was uniformly present. Right ventricular preponderance was revealed by the electrocardiogram in all patients. The size of the cardiac shadow varied in the roentgenograms, but there was usually prominence of the pulmonary artery segment. Six patients showed evidence of bidirectional shunts and one showed only a reversed shunt, while the data were insufficient for the determination of this point in the remaining three. Three patients were operated on, with a satisfactory result in one, a 16-month-old infant, in whom a biopsy of the lung taken in the course of the operation revealed only minimal pulmonary arterial changes. Forty-five cases of patent ductus arteriosus with reversal of flow were collected from the literature. Most of them were in adults. Twenty-two patients were operated on, with good results in four, three of whom were children.

Patent ductus arteriosus with reversed flow must be differentiated from interventricular septal defect (Eisenmenger complex in particular), idiopathic primary pulmonary hypertension, interatrial septal defect, mitral stenosis, tetralogy of Fallot, chronic pulmonary disease, atrioventricular canal, truncus arteriosus, and single ventricle. The safest and simplest diagnostic test is the determination of oxygen saturation of samples of blood obtained simultaneously from the right brachial and femoral arteries. Angiocardiography and cardiac catheterization also provided helpful information. The diagnosis of reverse patent ductus arteriosus is not difficult to make if the entity is kept in mind. Patent ductus arteriosus with reversal of flow can no longer be considered rare. Surgical treatment of the condition has been very disappointing, especially in adults. There is reason to believe that surgical intervention very early in life may arrest or reverse the development of pulmonary changes, which contribute largely to the high surgical mortality in the older age groups; surgical treatment may thus yield a higher salvage rate.

Endocardial Fibroelastosis in Infants Associated with Thrombosis and Calcification of Arteries and Myocardial Infarcts.

W. A Thomas, K. T. Lee, M. H. McGavran and E. R. Rabin. New England J. Med. 255:464-468 (Sept. 6) 1956 [Boston].

The autopsy protocols and microscopic sections from two infants who had died with myocardial infarcts resulting from advanced disease of the coronary arteries with calcification were studied in an effort to obtain some clues to the cause and pathogenesis of the disease. The material from these patients was also compared with that from 24 infants with uncomplicated endocardial fibroelastosis, 2 infants with the left coronary artery arising from the pulmonary artery, 1 infant with endocardial fibroelastosis complicated by mural thrombosis and myocardial infarcts without calcific arterial lesions, and 5 rabbits with myocardial infarcts resulting from thromboembolism. The two infants with calcific arterial disease and myocardial infarcts were found to have in addition endocardial fibroelastosis (characterized by fibroelastic thickening of the endocardium of the left ventricle and cardiac hypertrophy), an association not previously reported. Both of these diseases are uncommon, so it is unlikely that they were associated only by chance. Consideration of various ways in which the relation between the two diseases might be explained led to the conclusion that the most likely possibility was that the endocardial fibroelastosis was the underlying process and that the arterial disease and myocardial infarction resulted from thromboembolism.

Copper Deficiency in Infants: A Syndrome Characterized by Hypocupremia, Iron Deficiency Anemia, and Hypoproteinemia.

P. Sturgeon and C. Brubaker. A. M. A. J. Dis. Child. 92:254-265 (Sept.) 1956 [Chicago].

Sturgeon and Brubaker report on five infants in whom hypocupremia and hypoproteinemia were associated with iron deficiency anemia. At the time of diagnosis the patients ranged in age from 6½ to 9 months, with the exception of one, who was 2½ years old. All had in common a mild degree of edema and pallor. All had moderate anemia, microcytosis, and profound reduction in the concentrations of serum iron and serum copper. The total serum iron-binding capacity was not increased. The serum protein concentration was reduced in all cases. There was no laboratory evidence of renal or hepatic dysfunction. The authors believe that since these children had subsisted on a milk diet to the exclusion of practically all other foods, nutritional inadequacy may have played a part in producing the described syndrome. Preliminary therapeutic tests indicate that the various deficiencies can be corrected simultaneously with an improved diet and that, independently of the other deficiencies, the hypocupremia can be corrected with the oral administration of copper sulfate.

OTOLARYNGOLOGY

The Nasal Entrance in Relation to Nasal Function.

J. E. Poulin. J. Maine M. A. 47:274-275 (Sept.) 1956 [Portland, Maine].

Respiration is influenced to a great extent by the relative size of the nostril. The size and position of the anterior nares is determined by the character of the nasal tip and its surrounding anatomic structures. A deflection of the air current by a collapsed, twisted, or depressed nasal tip can in turn influence the size and position of the nasal entrance and in so doing affect the nasal physiology. The number of nasal tip deformities that are congenital in origin is small in comparison to the number produced by nasal injuries. Many of the injuries occur among children in infancy and early childhood and go unrecognized. A trivial blow on a child's nose resulting from a fall will often displace the tip of the cartilage in its septum. These accidents are frequently disregarded by the parents, and the unfortunate child has a displaced tip cartilage that becomes worse as time goes on. The incidence of neglected nasal injuries in the adult male is much greater than it should be. It is especially common among boys who participate in dangerous sports such as hockey, basketball, and football. Boys often accept a nasal injury as a part of the game and do nothing about it until they experience difficulty in breathing in later years. It is of the utmost importance to make certain that nasal trauma has not involved the tip of the nose, but if it has, proper steps should be taken to correct it as soon as possible.

Significance of Allergy in Persistent Respiratory Infection.

A. Dintenfass. A. M. A. Arch. Otolaryng. 64:171-177 (Sept.) 1956 [Chicago].

An attempt is made to demonstrate the close association and interdependence of respiratory-tract infection and allergy and the need for a thorough understanding of both allergic and surgical principles in order to obtain maximum therapeutic benefits. The association of allergy and infection affects all parts of the respiratory tract, producing diverse but characteristic pathological patterns in the nose, paranasal sinuses, Eustachian tubes, each of the anatomic divisions of the ear, and the bronchial tree. The underlying physiological and pathological processes are described. Efficient treatment is dependent upon adequate study of the allergic state. The offending allergens must be avoided or used in desensitization. Properly selected and timed surgical procedures in conjunction with allergic therapy provide maximum improvement and more permanent relief. Representative case histories illustrate the essential principles involved.

THERAPEUTICS

A Clinical and Bacteriologic Evaluation of Novobiocin in Seventy-Five Patients.

J. Z. Pearson, A. Somberg, I. Rosenthal and others. A. M. A. Arch. Int. Med. 98:273-283 (Sept.) 1956 [Chicago].

Novobiocin is a new antibiotic produced by a species of Streptomyces and discovered almost simultaneously by two independent groups. The authors used novobiocin in 75 patients, of whom 9 had either leukemia or polycythemia; they were followed with leukocyte counts, platelet counts, and hematocrit readings to see whether a drop in any of these indices would occur while novobiocin was being administered. Pretreatment cultures were obtained from all of the 66 patients with infections. Novobiocin (Albamycin, Cathomycin) was given orally, either in capsule form or in suspension, and the daily dose was 30 mg. per kilogram of body weight in children or 2 gm. in adults.

The response in infections with Micrococcus pyogenes var. aureus (staphylococci) was generally good except in cases where chronic tissue changes predisposed to continued infection. Improvement was noted in patients with pneumococcic and β-streptococcic infections, but the response was often not so prompt and the eradication of the organism not so consistent as in cases in which penicillin is used. No improvement was observed after administration of novobiocin to patients with infections caused by Enterococcus or Proteus organisms or in patients with actinomycosis or lung abscess. The median serum concentration of novobiocin after a standard dose was from 64 to 128 mcg. per milliliter, but there was wide variation. Untoward reactions were observed in 14 (18.7%) of the patients. Skin eruptions occurred in 12, eosinophilia in 5, leukopenia in 2, and jaundice in one. Eight of the patients were given a second course of novobiocin, and in five of these toxic signs or symptoms reappeared. Reactions to both proprietary forms of novobiocin (Albamycin, Cathomycin) were observed in two of the four patients to whom both were given. Strains of micrococci (staphylococci) resistant to novobiocin appeared in four patients treated for three months or longer.

Successful Treatment of Gonococcic Endocarditis with Erythromycin: Review of the Literature. D. S. Davis and M. J. Romansky. Am. J. Med. 21:473-480 (Sept.) 1956 [New York].

The authors report on a 23-year-old Negro woman in whom polyarticular arthritis developed during pregnancy five years after a probable primary gonorrheal infection. Under observation a systolic murmur first appeared and later became changing in character. A diastolic murmur also made a transient appearance. Coincident with the onset of murmurs, skin lesions of probable embolic nature appeared on the extremities. One of 10 cultures obtained during the initial period of observation yielded a growth of Neisseria gonorrhoeae, thereby confirming a diagnosis of gonococcic endocarditis. Specific therapy consisted of a total of 108 gm. of erythromycin administered orally and intravenously over a 32-day period. No growth was observed in nine blood cultures obtained during this course of treatment, and single blood cultures obtained on the fourth, sixth, and seventh days after cessation of therapy were negative. Marked objective and symptomatic improvement occurred during hospitalization lasting 53 days. Two and a half months later the patient was delivered of a healthy child without further untoward event. When last seen 10 months after the onset of her illness, the patient was still in excellent health. This is the first report of erythromycin therapy of gonococcic endocarditis.

Coumadin (Warfarin) Sodium: A New Anticoagulant. J. H. Nicholson and T. Leavitt Jr. New England J. Med. 255:491-501 (Sept. 13) 1956 [Boston].

Coumadin sodium is a monocoumarin compound, in contrast to Dicumarol, which is, as its name suggests, a dicoumarin compound. Unlike Dicumarol, cyclocumarol, Tromexan, and phenindione, Coumadin forms a stable sodium compound. The sodium derivative is soluble in water and forms stable solutions that can be administered parenterally. Its reported effectiveness by the oral, intravenous, intramuscular, or rectal route may reside in this property. The authors used this drug for acute thromboembolic episodes and prophylactic therapy in 100 patients in private practice and on the wards of the Lawrence General and Bon Secours hospitals. Coumadin sodium (Link's warfarin sodium) was given intravenously and orally. The induction of therapeutic hypoprothrombinemia (level of 35 to 10%) was relatively prompt. The use of heparin was limited to patients with pulmonary embolism, who received only about three or four doses of heparin. The initial dose averaged about 60 mg., and the daily maintenance dose by the continuous or intermittent method, based on daily prothrombin determinations, was about 10 mg. The maintenance dose, which was readily established, was generally consistent from day to day in the same patient. Fewer periods of "escape" from the therapeutic range occurred than with other anticoagulant drugs the authors had used.

Hemorrhagic phenomena, attributable to the drug, occurred in five patients (three had bleeding episodes and in two subcutaneous petechiae developed). Bleeding occurred only in patients who had undergone surgical treatment, and it subsided promptly after administration of phytonadione. No fatality was caused by the drug. These experiences and others reported in the literature indicate that Coumadin (warfarin) sodium is a more nearly ideal anticoagulant drug than any of its congeners now available. The drug deserves wide clinical application in thrombotic and thromboembolic disorders.

Effects of Tetrachlorethylene Without a Purge, Followed by Ferrous Sulfate in Ancylostomiasis. A. R. Pinto, F. C. Costa, L. V. deMeira and J. P. Viana. Am. J. Trop. Med. 5:739-741 (July) 1956 [Baltimore].

In 1954 it was demonstrated by Carr and co-workers in the Dominican Republic that tetrachlorethylene is more effective in the treatment of ancylostomiasis when it is not followed by a saline purgative. Pinto and associates tried this method in 165 patients in Portuguese West Africa. They found that the omission of the saline purge after treatment of hookworm infection with tetrachlorethylene increases the effectiveness of the drug, shortens the time of treatment, lowers its toxicity and cost, facilitates the administration of mass treatment, and improves the possibility of curing the disease.

PATHOLOGY

Immediate Passage of Tumor Cell Emboli Through the Liver and Kidney. I. Zeidman, W. J. Gamble and W. L. Clovis. Cancer Res. 16:814-818 (Sept.) 1956 [Chicago].

Experiments were made to ascertain whether or not tumor cell emboli could pass unarrested through the liver and kidney. The transplantable V$_2$ carcinoma was used in domestic rabbits and, in rats, transplantable Flexner-Jobling carcinoma, Murphy-Sturm lymphosarcoma, Lewis fibroma, and Lewis lymphoma. For transhepatic studies, tumor suspension was injected into the portal vein, and simultaneously blood was drawn from the vena cava just above the liver. The blood was then injected intravenously into a second animal. The development of tumors in the second animal indicated immediate transhepatic passage of tumor cell emboli in the first animal. In transrenal studies, tumor suspension was injected into the aorta above the kidneys, the blood was collected simultaneously from the renal vein, and this blood was injected intravenously into second normal animals. Immediate transhepatic and transrenal passage of tumor cell emboli occurred with all tumors used except the Flexner-Jobling. The incidences of such passage varied, being higher in tests with lymphoma cells. It is concluded that tumor cell emboli can pass unarrested through the circulation of both liver and kidney.

This report is one of a series dealing with the passage of tumor cell emboli through the circulatory bed of various organs. The problem was to determine whether or not tumor cells, circulating in the blood, may pass immediately through an organ, perhaps to lodge in a more distant organ. If so, this might account for some peculiarities in the distribution of metastases. For example, human cancers of the gastrointestinal tract occasionally metastasize to the lungs without producing visible liver metastases. Previously, it had been thought that this pattern of metastasis depends upon lymphatic and thoracic duct spread.

RADIOLOGY

Giant-Cell Tumors and Roentgen Treatment. S. Marzolla. Minerva med. 47:357-365 (Aug. 11) 1956 (In Italian) [Turin, Italy].

The author reports on nine patients with giant-cell tumor of bones who received radiological treatment. Five cases were controlled for many years. Very good results followed in all cases. The treatment gives good functional results and reduces to a minimum the danger of relapse. Doses must be moderate, because high doses may interfere with the rebuilding of the bone. The process of recovery is slow but certain. One sign of recovery not previously discussed in the literature is the diminution of transparency in the lacunar areas of the tumor before the deposition of calcium salts takes place. When recalcification starts, it proceeds slowly but steadily. A return to the normal architectural pattern of the bone cannot be expected; it will suffice to have a bone that is strong, solid, and resistant.

BOOK REVIEWS

Sports Injuries Manual for Trainers and Coaches. By Donald F. Featherstone. Foreword by R. Salisbury Woods, M.D., F.R.C.S. Cloth. $6. Pp. 132, with 24 illustrations. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1956.

In his introduction, the author says that, although there may be some disagreement regarding the advisability of teaching the treatment of injuries to laymen, athletic trainers and coaches who are not medically qualified will, nevertheless, continue to treat most sports injuries. He has, therefore, designed this compact manual of reference to indicate to the layman not only correct management but also the limits beyond which the services of a physician are absolutely required. In point of fact, most physicians who are called on casually to treat sports injuries, although they may be familiar with the anatomic derangement and are able to offer effective first aid and immediate treatment, probably know less about the prevention and long-term management of these injuries than the experienced trainer or coach. Every general practitioner and surgeon would do well to familiarize himself with the principles involved in the total treatment of these injuries, since there are lessons to be learned here in regard to the shortening of periods of disability and the preservation of function that can be applied to the treatment of injuries from other causes.

The first part of the book is devoted to a concise, accurate, and easily comprehensible explanation of the basic anatomy and physiology of the human body. Particular emphasis is placed on the principal muscle groups and their actions. The second part is devoted to the basic knowledge and equipment the trainer must have to be prepared to aid the injured athlete. The third part discusses methods of prevention; and the fourth part, the treatment of strains, sprains, contusions, abrasions, and lacerations and skin infections. There is a short chapter on the more serious injuries, emphasizing immediate medical assistance; there is also a chapter on miscellaneous injuries. Since the author is English, the American reader will find some unfamiliar medicaments and methods of management recommended. Placing the blame for some muscle strains on the presence of systemic foci of infection seems a little outdated. Certainly most surgeons and orthopedists would not approve as adequate treatment for a Bennett fracture the strapping of the injured hand with elastic adhesive tape. Also, current thinking about the origin and spread of dermatophytosis does not favor the prophylactic use of foot baths containing a mild antiseptic solution. The illustrations are good but few in number. In general, the advice offered is practical, sensible, and based on wide experience. This book can be particularly recommended to physicians who attend high school and college athletes, as well as to the coaches and trainers for whom it is intended.

Corneal Grafts. Edited by B. W. Rycroft, O.B.E., M.D., D.O.M.S. With foreword by Sir Cecil Wakeby, K.B.E., C.B., LL.D Cloth. $13.50. Pp. 286; 13, with 155 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3; Butterworth & Co., Ltd., 88 Kingsway, London, W.C.2; 1367 Danforth Ave., Toronto 6, Ontario, Canada, 1955.

The chapters in this book on the anatomy and physiology of the cornea and the ultrastructure and chemical composition, with a discussion on the mucoids, salts, and metabolism, are all worthy of the reader's critical attention. Francois and Rabaey (1953) stated that the disappearance or the decrease of the mucoid substance of the stroma promotes vascularization. Neovascularization is still the mortal enemy of the corneal graft, and, when its causative factor or factors become known, a great step toward the elimination of corneal opacification will have been made. The pathology of corneal opacities is thoroughly described, with the aid of excellent photomicrographs. Paufique, the father of lamellar keratoplasty, states that the old prejudice against lamellar keratoplasty was based on the unavoidable opaque connective tissue formed behind the graft. He claims that this is now avoidable, due to the progress in asepses, advances in technique, and the use of antibiotics. He carefully describes and beautifully illustrates the technique of partial lamellar keratoplasty, using some of the instruments that are more often used in Europe than in the United States. He enumerates the postoperative complications of lamellar keratoplasty and their treatments now in vogue in Europe.

Some of the special methods as described by Sourdille, particularly the mushroom graft of Franceschetti with his apparatus, are given in detail. The general complications of corneal grafting are discussed by Tudor Thomas, who points out that gray streaks and haze of the donor cornea are likely to produce vascularization of the cornea and opacity. The use of citrated saline solution lessens the tendency of the iris to become adherent to the graft and is without danger, especially when the cornea shows only slight vascularization. Another important highlight of this chapter is the discussion of the treatment with antihistamines in the first two weeks. This is advocated to lessen the chances of any reaction to antigens contained in the corneal tissue. Frederick Ridley makes an important practical point in the preoperative temporary fitting of contact lenses. This procedure can be used to make a direct comparison between the apparent thickness of the cornea and the contact lens in the slit-lamp beam. This is of exceptional value where lamellar keratoplasty is contemplated. Dr. Marc Amsler introduces a valuable clinical procedure that is not generally done in the United States: a diagnostic puncture of the anterior chamber and the examination of the aqueous humor for its protein content and the enumeration of its cells. The presence of numerous cells indicates that inflammation of the uveal tract is still active, particularly if these cells are lymphocytes or even polymorphonuclear leukocytes. Dr. Amsler correctly states that, if perforating keratoplasties were always preceded by a careful study of the aqueous humor, they would present fewer disagreeable surprises for the surgeon, such as postoperative inflammations and secondary glaucoma. He also points out that keratography is useful for the study of asymmetrical and irregular curvatures of the cornea; it reveals the form that the graft takes once it is incorporated into the recipient cornea. Keratography offers an objective standard paralleling the subjective criterion of the visual acuity with the final operative result.

Under Methods of Preserving Tissue, Buschke (1951) states, "Since the stromal cells of the graft have to be alive at the time of its transplantation, storage methods entailing chemical preservation, freeze-drying, or quick-freezing in the absence of glycerol, merit no further consideration, since cells are known not to survive these treatments." The chapter on special instruments, corneal markers, and splints gives special attention to instruments used in Europe. Dr. Rycroft presents exhaustive reports on corneal grafts, as contained in the chapters by outstanding European pioneers, and has supplemented them with his own results and the reports of outstanding American ophthalmologists. The book is readable and amply illustrated. It should be in the library of any ophthalmologist who wants to keep up with what is happening in this field in Europe.

Currents in Biochemical Research 1956. Edited by David E. Green. Twenty-seven essays charting present course of biochemical research and considering intimate relationship of biochemistry to medicine, physiology, and biology. Cloth. $10. Pp. 697, with illustrations. Interscience Publishers, Inc., 250 Fifth Ave., New York 1; 88-90 Chancery Lane, London, W.C.2, England, 1956.

This volume records some of the work done by 32 authors in many important fields in biochemical research. The intent of the book, as stated by Dr. Green in the preface, was to give an over-all picture of the present status of significant problems in a particular field, to point out the present broad strategy used in attacking these problems, and then to speculate as to the paths most likely to be followed in future research. Much of the progress made on the many problems in biochemistry has been due to the development of new techniques in the isolation,

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

identification, and further characterization of biochemical substances. Such techniques include paper chromatography, spectrophotometry, electrophoresis, and the use of isotopes. In reading the various chapters, one is immediately impressed with the tremendous advances that have been made since the first volume was written 10 years ago. A glance at the titles of these essays suggests the vast amount of work that has been done in various phases of the enzyme study. A thorough reading of the book reveals even more the many related fields into which the study of enzymes has spread. At least eight of the essays are concerned directly with various general espects of enzyme chemistry, and most of the others devote a major portion of their material to more specific enzymes or enzyme systems. Included are such general topics as enzyme kinetics, enzyme complexes, induced enzyme formation, enzymes as reagents, enzymes in electron transfer, special problems in multiple enzyme systems, and the relationship between enzymes, coenzymes, nucleotides, and prosthetic groups.

Other relatively specific topics include a discussion on certain biochemical aspects of virus growth, bacterial fermentation, vitamin and growth factors, hormones, ribonucleic acids, porphyrin biosynthesis, sugar interconversion in nature, muscular and nerve activity, blood functions, and carcinogenesis. Subjects of a more general nature that are covered include problems of cellular biochemistry, biochemical problems in disease, chemical structure, and biochemical questions. Essays on various general aspects of protein structure and on the structure of insulin are also included. Each of the essays includes a bibliography. As shown by the varied subject matter presented, the field of biochemistry is broad and complex. It borders on genetics, cytology, physiology, and theroretical chemistry. Much of the material should be of interest to physicians.

Cytology of the Blood and Blood-Forming Organs. *By Marcel Bessis, Director of Research Laboratory, Centre national de transfusion sanguine, Paris, France. Translated by Eric Ponder. Cloth. $22. Pp. 629, with 405 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 99 Great Russell St., London, W.C.1, England, 1956.*

Since its inception, morphology has been the cornerstone of hematology, and hematology, which was once a rather drab subject, has expanded into physiopathology, immunology, and chemistry. Despite this, the cell has retained its preeminence due largely to the development of neomorphology. At one time, morphological studies were represented simply by the use of blood and bone marrow smears stained with one of the Romanowsky stains. In recent years, phase microscopy has allowed the observation of unstained material in the cell that is unseen with staining techniques. All manner of cytochemical methods have been developed for studying specific enzymes and other chemical materials in the cell. The motion picture technique, particularly with the use of time lapse has been developed to a high degree for the study of the actual life and death of a cell. Finally, electron microscopy has opened the door to the observation of materials within the cell consisting of only a few molecules. In all of these advances the author has pioneered, and, in fact, he has created in this book a new framework of morphological hematology. His remarkable phase microscopy pictures, his extraordinary electron microscopy, and his research with the aid of motion pictures have become well known to hematologists, particularly those with a knowledge of French. This book should serve to introduce his work to many English-speaking readers. Eric Ponder has done a fine job of translation. Dominating the book are the extraordinary electron and phase contrast photomicrographs of blood cells, which give a new dimension and insight into minute cellular structures. This English translation is an excellent reproduction of the original French treatise published in 1954; in addition, in many areas the text is greatly expanded, particularly in the fields of platelets, megakaryocytes, and electron microscopy. Orthodox morphology is by no means neglected, but neomorphology is here in full force and beauty. The book is excellently printed, the type is legible, and the photomicrographs are superb. Despite its high price, the book is a necessity for all those who work in the field of hematology.

Progress in Clinical Obstetrics and Gynaecology. *By T. L. T. Lewis, M.B., B. Chir., F.R.C.S., Obstetric Surgeon, Guy's Hospital, London, England. Cloth. $12. Pp. 594, with 90 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; J. & A. Churchill, Ltd., 104 Gloucester Pl., Portman Sq., London, W.1, England, 1956.*

This book is designed to put in concise form the present knowledge of various conditions in the field of obstetrics and gynecology. Each chapter considers one problem. With such broad coverage, it is inevitable that the subjects are discussed in a condensed fashion. The author emphasizes things of practical significance at the expense of more basic studies of equal importance. He has also chosen to build up the data behind what are apparently his own conclusions. The British viewpoints and work are stressed, which makes it surprising to find, for example, such incomplete reports as those dealing with the anemias of pregnancy. The discussions of some of the malignant diseases are so condensed as to be grossly incomplete. There are some references at the end of each chapter; but these give altogether too much stress to the British literature, which in itself is incomplete, and almost none to the non-English-language literature. There is no reference to any studies by the author himself. The book does not, then, carry the authority of a reference book but is designed as a superficial but quick source of practical information for postgraduate teaching rather than as a book for graduate study. It is not an adequate source, as the author admits, for the specialist. It is well printed, with few typographical errors, on glossy paper. There is a moderate number of illustrations. The language is clear and concise. There is a good index. The book is recommended for the general practitioner doing work in obstetrics and gynecology, for the intern, and for those who need to understand the British approach to these practical problems. Subsequent volumes should limit the number of subjects to be considered and discuss them in greater detail.

The Premarital Consultation: A Manual for Physicians. *By Abraham Stone, M.D., Associate Clinical Professor of Preventive Medicine, New York University College of Medicine, and Lena Levine, M.D., Associate Medical Director, Margaret Sanger Research Bureau, New York. Cloth. $3. Pp. 90, with 11 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 99 Great Russell St., London, W.C.1, England, 1956.*

As is stated in the introduction to this book, premarital counseling is an extension of preventive medicine in the family unit. That it is important would seem to be an indisputable fact, yet, unfortunately, far too many physicians tend to shrug it off as something that has nothing to do with medicine. Inquirers are referred to psychologists or marriage counseling agencies that, even though admittedly providing excellent services, still cannot give the all-inclusive guidance the physician can and should offer. As the authors point out, this type of assistance is not beyond the scope of the general practitioner, despite the tendency to assign it to various specialty fields. After instructions on taking a premarital history and making necessary examinations are given in the manual, there is a chapter, which gives extensive guidance, dealing with interview of the couple. Interspersed throughout this chapter are questions and answers exchanged by the three participants. Information is provided on sexual adjustment, family planning and contraceptive methods, social and emotional factors in marriage, and the physiology of sex. This is followed by a brief and simplified discussion of genetics, with specific consideration of mental defects, epilepsy, and other rather common conditions. Especially helpful are sections in the appendix dealing with use of the vaginal diaphragm, marriage laws of the states, and birth control laws. This volume should be of interest and assistance to many physicians.

Accidental Poisoning in Childhood: A Reference-Guide to the Chemical Constituents of Common Household Substances, Together with Treatment Recommendations for Their Accidental Ingestion by Children. *Prepared by Committee on Accident Prevention, American Academy of Pediatrics, and written by Edward Press, M.D., M.P.H., Field Director, American Public Health Association. Cloth. $3. Pp. 131. American Academy of Pediatrics, 1801 Hinman Ave., Evanston, Ill.; published by Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill., 1956.*

In 1950, the American Academy of Pediatrics took official notice of the problems and hazards of poisoning by appointing a committee on accident prevention. Dr. Edward Press, working through this committee has now compiled a summary of the literature on the constitution of various household chemicals and methods of treatment. This booklet is divided into three main sections: Treatment Procedures, List of Toxic Substances and

Suggested Treatment, and Toxic Constituents of Household Products. For quick reference, these three sections have been set off from one another by pages of a different color. Since this booklet was compiled primarily to aid in treating children who have accidentally ingested household poisons, much of the recommended treatment is broken down into dosages for infants and young children. The author has also pointed out that the suggestions given are only a guide and "must not be used mechanically or one will slip into sloppy and ineffective 'slide-rule' medicine." Since it is almost physically impossible to include up-to-date information on the ingredients of all household products, the author has chosen to include a number of representative items. He has, however, included a list of references that may be consulted for additional information. Despite the fact that the scope of the book is limited to household poisons, its clarity of style and ease of reference provide an excellent guide for the physician who is called on to treat all types of accidental poisoning in children.

Surgery for General Practice. By Victor Richards, M.D., Professor of Surgery, Chairman of Department of Surgery, Stanford University School of Medicine, San Francisco, California. Cloth. $17.50. Pp. 947, with 476 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1956.

This textbook is a unique contribution. The author drew on his associates working in specialized fields in the same clinic, and the experiences cover a span of many years. The concept of treating the total patient rather than a diseased segment of his body is continually emphasized. The subjects discussed include local anesthesia, hemorrhage, shock, injury, surgical infection and chemotherapy, anticoagulants, burns, plastic surgery, tumors, surgical disorders of all parts of the body, hypertension, intractable pain, peripheral nerve surgery, and fractures. The limits of a textbook for general practitioners are difficult to define with accuracy. The underlying philosophy of the author in emphasizing the obligation to treat the whole patient is commendable. One may envision a simple problem initially, but it may rapidly become complicated. The author, therefore, has encompassed in this book methods of surgical treatment that will conduct patients safely through problems of changing complexity. The author has intentionally omitted a bibliography. This is not a book of operative techniques but one emphasizing the principles of surgery for the average physician. The tables, diagrams, and line drawings are effectively placed, precise, clear, and unusually illuminating. This book should be found high on the roster of timely and outstanding contributions. Every physician should have the fundamental surgical knowledge it presents.

Urology. By B. G. Clarke, M.S., M.D., F.A.C.S., Associate Professor of Urology, Tufts University School of Medicine, Boston, and Louis R. M. Del Guercio, M.D., Assistant Resident Surgeon, St. Vincent's Hospital, New York. Cloth. $6.50. Pp. 245, with 163 illustrations. Blakiston Division, McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 36; 95 Farringdon St., London, E.C. 4, England, 1956.

This book is intended to give a brief presentation of the subject matter of special urologic interest to the undergraduate student and the general practitioner. It has a well-arranged short essential text complemented by a sufficient number of line drawings, diagrams, and pictures to partially replace lengthy detailed descriptions. As the authors remark, "For the leisurely reader, this material amplifies the text in much the same way as a series of short clinics on the commoner urogenital diseases." A selected list of references is provided with each chapter. Of the many textbooks on urology published in the past few years, this one is most suitable for the classroom work of the undergraduate student. There are some apparent omissions. Pneumaturia in a person with diabetes or pneumaturia associated with an enterovesical fistula is not mentioned. The discussion on the differential diagnosis of bladder tumors does not mention the necessity for recognizing irradiation granulomas, inflammatory areas, surrounding enterovesical fistulas, foreign bodies, or areas of encrusted cystitis. The importance of diabetes as a cause of renal papillary necrosis and persistent urinary infection is omitted. The character of the book suggests that the experience of the authors has been largely one of hospital care, with a paucity of reference to the more common genitourinary conditions that are seen in routine office practice.

Rosenau Preventive Medicine and Public Health. By Kenneth F. Maxcy, M.D., Dr.P.H. With 27 contributing authors. Eighth edition. Cloth. $15. Pp. 1465, with illustrations. Appleton-Century-Crofts, Inc., 35 W. 32nd St., New York 1, 1956.

This second revision of Rosenau's widely used textbook to be compiled by Dr. Maxcy appears five years after the previous edition. In that time Dr. Maxcy has retired from his chair in epidemiology. The words "public health" have replaced "hygiene" in the title. This was done to give better indication of the scope and purpose of the book, which remain unchanged. There has been no change in the list of contributors. The author states that about 44% of the text has been revised to bring it up-to-date. The length of the text has not been increased, but a more adequate index has been provided. The addition of such subjects as Coxsackie virus and adenovirus infections, epidemic nephritis, and West Nile encephalitis without increasing the size of the book has been accomplished by condensing some of the older material, omitting some of the graphs and tables, and in a few pages setting the lines closer together. The revision of the sections on tuberculosis and ionizing radiations was especially well done, and the latter is a matter of increasing interest. This book continues to be the outstanding work in its field. It contains much information that should be of value to the general practitioner and is an indispensable item in the library of the public health specialist.

The Morphology of Human Blood Cells. By L. W. Diggs, M.A., M.D., Professor of Medicine and Director of Medical Laboratories, University of Tennessee and City of Memphis Hospitals, Memphis; Dorothy Sturm, Instructor, Memphis Academy of Arts; and Ann Bell, B.A., Instructor in Medicine, University of Tennessee. Cloth, loose-leaf. $12. Pp. 181, with 54 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, England, 1956.

This textbook, presented in atlas form, approaches the study of blood cells from the developmental and structual point of view rather than from that of the specific disease entity. The authors are to be commended on this emphasis, for a sound knowledge of the basic difference between normal and pathological cells is of great clinical value. The illustrations, in a separate section for easy reference, are of exceptional quality and are well integrated with the accompanying text. The use of commonly applied synonyms in addition to the standard terminology sponsored by the American Society of Clinical Pathologists and the American Medical Association, and the indexing of all terms, adds to the value of this reference book. The section on techniques and methods provides a useful review of these procedures, rather than a basic set of instructions, and describes some of the less common but occasionally needed stains. More could have been included on bone-marrow procedures. While the authors have prepared the book primarily for medical students and student technologists learning about blood cells for the first time, the text, perhaps due to its brevity, appears to require a substantial histological background. The book should be of value to the practicing physician who makes his own examination of blood smears.

The Recovery Room: Immediate Postoperative Management. By Max S. Sadove, M.D., Professor of Surgery (Anesth.) and Head, Division of Anesthesiology, University of Illinois College of Medicine and Research and Educational Hospitals, and James H. Cross, M.D., Clinical Assistant Professor in Surgery, University of Illinois College of Medicine, Chicago. With contributions by 24 authorities. Cloth. $12. Pp. 597, with illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, England, 1956.

Twenty-six persons have contributed to this book. They have attempted to discuss in great detail the postoperative management of patients in their institutions who have undergone various procedures. The most extensive chapter deals with the management of circulation, shock, respiration, and nutrition. This book should be of value to an institution that desires to set up a recovery room, and it should be useful as a means of evaluating a recovery room already in existence. Moreover, the book should be instructive to surgeons who do not have the facilities described but who might wish to use some of the measures advocated in the postoperative care of patients. The book is well indexed, is printed on excellent paper, and is illustrated extensively. The sources of some of the illustrations are not adequately indicated by the authors.

QUERIES AND MINOR NOTES

SIDE-EFFECTS OF STEROID THERAPY IN CHILDREN

To the Editor:—*What undesirable side-effects have been reported from the use of steroid therapy (corticotropin, cortisone, prednisone) in the treatment of children over a short period of time and in long-range therapy? There appears to be considerable apprehension in the use of the steroids in growing children.* *George L. Popkin, M.D., Rockville Centre, N.Y.*

Answer.—The undesirable side-effects of pharmacological courses of steroid therapy in children over a short period of time are largely those concerned with potassium deficiency and salt retention, with resulting edema. When administered over long periods of time, steroids may reduce the individual's resistance to infection by inhibiting antibody formation and by increasing the dissemination of bacteria or viruses through the tissues to such an extent that he is made more vulnerable and fails to show any clinical evidence of response. For these reasons it is thought fatal cases of chickenpox (varicella) occur in children who are receiving this form of therapy. Again, steroid therapy may change the clinical picture of chickenpox to such an extent that diagnosis is difficult, i. e., by altering the appearance of the dermatological manifestations, or it may permit the rash to continue to occur in characteristic "crops" over a period of four to five weeks.

Untoward effects have also been reported among children with pulmonary tuberculosis, and there is a steadily increasing feeling that herpes zoster and ophthalmia are aggravated by either oral or local use of steroids. The administration of cortisone to hamsters and monkeys prior to infection with the virus of poliomyelitis changes nonparalytic to paralytic poliomyelitis. Prolonged steroid therapy may so usurp the function of the adrenal glands that they may not resume their normal activity when the agent is withdrawn for an indefinite period. Thus, corticotropin may logically be used at the end of prolonged steroid therapy, with gradually decreasing doses. To these effects must be added the "moon face," obesity, and pigmentation of adrenal cortical hyperfunction (Cushing syndrome).

SUDDEN DEATH

To the Editor:—*I was consulted by the coroner concerning the death of a woman who allegedly had been hit in the abdomen by the blunt side of an ax. Death was almost instantaneous. Autopsy revealed no marks on the body, and the findings were negative except for those of acute alcoholism. Is it possible that cardiac arrest could have been instituted by a severe blow over the solar plexus without leaving any telltale marks on the body?* *M.D., North Carolina.*

Answer.—Many cases are on record of acute fatal circulatory failure after injuries that would not ordinarily be regarded as dangerous. Thus, a blunt impact over the solar plexus, precordium, or a testis, pressure on the carotid sinus, or sudden dilatation of the rectum may be immediately fatal. Postmortem examination in such circumstances may disclose no gross or microscopic evidence of trauma. The mechanism responsible for such a death may be vagocardiac inhibition or reflex systemic vasodilatation.

In evaluating such a situation, it should be borne in mind that a person may die unexpectedly and suddenly from natural causes without any postmortem evidence as to the nature of the fatal disease. Thus, a sudden death should not be attributed to cardiac arrest or to reflex vasodilatation due to a blunt impact unless (1) the occurrence of the impact was well documented and (2) a complete postmortem pathological and toxicologic examination failed to disclose the cause of death.

HYPOCALCEMIA IN INFANTS

To the Editor:—*I would appreciate information regarding hypocalcemia with laryngospasm in newborn infants, with particular reference to the incidence between breast-fed and formula-fed babies. Is a commercially prepared formula more prone to giving rise to this condition?*

Boyd C. Hindall, M.D., Lake Geneva, Wis.

Answer.—Laryngospasm is one symptom of hypocalcemia. It is usually accompanied by other signs of tetany, such as carpopedal spasm. It must be differentiated from laryngeal stridor and trauma due to too energetic aspiration of the pharynx in newborn infants. Tetany usually occurs in formula-fed babies and rarely in breast-fed infants. Breast milk has a calcium phosphorus ratio of about 2:1, while cows milk has about a 1:1 ratio. This high phosphorus ratio, combined with hypofunction or immaturity of the parathyroids, seems to be the cause of tetany of newborn infants. There is usually a low serum calcium level, below 6.5 to 7 mg. per 100 cc., and a high phosphorus level of over 6 mg. per 100 cc. Some commercial formulas are usually made from cows' milk, with a calcium-phosphorus ratio of about 1:1. It is recommended, when cows' milk is used as a prophylaxis against hypocalcemia or tetany in infants, that it be diluted 1:2 or 1:3 with water.

MENSTRUAL HEADACHES

To the Editor:—*A 32-year-old woman has had occasional mild to moderate headaches associated with her menses for several years. For the past couple of years these headaches have been occurring with increased frequency and increased intensity just prior to and/or during the menses. Powerful analgesics have given but slight relief. Are any other measures of value to help relieve this incapacitating symptom?*

M.D., Georgia.

Answer.—Some women with a similar complaint have been greatly helped by the administration of ammonium chloride. The patient should be asked to refrain from adding table salt to her food during the two weeks before the onset of the menstrual bleeding. During this time she should take 0.6 gm. of ammonium chloride three times a day. Another simple and effective agent is testosterone propionate. The patient may be given 25 mg. hypodermically on the 10th and the 3rd day before the expected menstruation, or, better still, she can take a 10-mg. tablet of methyltestosterone, or a 5-mg. tablet, sublingually or buccally, daily for 10 days before the expected onset of menstrual flow.

RIDGE OVER FOREHEAD OF YOUNG BOY

To the Editor:—*A boy, now 2 years old, has a disfiguring ridge over the frontal or metopic suture. This is associated and continuous, with a vertical white line over the middle of his nose. Several local pediatricians say it will disappear. However, this deformity, far from disappearing, has, I believe, become more prominent. His head appears to be abnormally long and narrow. This boy is a premature child. Is there anything that can be done to remove this deformity?* *M.D., Canada.*

Answer.—In the absence of further history and physical findings, especially developmental data, neurological findings, and the skull measurements, it is assumed for the purpose of this reply that such findings are normal. The long and narrow shape of the head is not unusual for a child of premature birth. Indeed, some clinicians feel they can frequently detect such children even in the school-age group. This head shape may persist or may eventually become less conspicuous, actually or relatively, as further head and body growth takes place. An osseous ridge palpable or visible over the metopic suture is also not uncommon in premature or full-term infants. When it occurs, it is more apparent in children with narrow heads. The ridge usually be-

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

comes less conspicuous in later years, since it is uncommon among older children and adults. A palpable ridge over the metopic and sagittal sutures in the presence of a long and narrow head might make one suspicious of craniostenosis of these sutures. An x-ray of the skull will rule out this possibility. Neurological findings may not be present until the child is 2 years of age or older. The vertical white line over the midline of the nose has been seen in some children. Its cause and significance are obscure. In the absence of pathological findings, therapy is not warranted for the bony ridge or the white line in the early years of the child's life. The proportionate differences in growth in the early years makes the head deformity more conspicuous, and in most instances it can be expected to become less apparent.

IDENTIFICATION OF THE BLIND

To the Editor:—*Please discuss conditions under which a blind person is identified in the United States. In Germany, a special band is worn on the left arm. In France and Belgium, a blind person is identified by a white cane. In Europe, conditions under which these marks of identification are distributed are the same everywhere: a person must have less than 10% of normal vision to be identified as blind. What are the conditions in the United States under which canes are distributed?*

Daniel M. Rolett, M.D., New York.

Answer.—There is no distinguishing mark by which blind persons are identified in the United States. In fact, there is a definite wish on the part of many blind persons to avoid being conspicuous, quite contrary to the desire of blind beggars who wear dark glasses in order to attract attention and obtain pity for their handicap. All states do have laws restricting the use of white canes to blind persons and, in general, giving blind persons certain rights of way in crossing streets and roads. These laws differ somewhat, and it is recommended that details be obtained by physicians from their own state or local agency for the blind.

DATING OF SEMINAL STAINS

To the Editor:—*Can the stains produced by dried semen be dated?*

M.D., Alabama.

Answer.—Dried stains produced by semen cannot be dated with any degree of accuracy. If seminal ejaculate is dried rapidly on a reasonably clean surface, the spermatozoa may remain intact, the antigenic properties of the fluid may persist, and its acid phosphatase may resist deterioration for many months. Thus, excellent preservation of cellular, immunologic, and chemical characteristics of the fluid does not necessarily indicate that the stain is recent, nor does their deterioration necessarily indicate that the stain is old.

HOSPITALIZATION FOR OVERWEIGHT

To the Editor:—*A recent article in the* New Jersey Medical Journal *states that patients more than 50 lb. (22.7 kg.) over their recommended weight who have failed to reduce on ambulatory treatment should be hospitalized for one to two weeks for good preventive medicine. Despite much additional authoritative evidence in the literature that confirms the value of this, some members of our hospital staff feel that a busy hospital should not waste bed space for such a condition; other members feel that encouraging hospitalization for such obese patients will actually save bed space by lessening the frequency of heart disease and other complications of obesity. We would appreciate an opinion.*

Leonard Casser, M.D., Cresskill, N. J.

Answer.—It is not possible to offer a categorical answer to this question, because of the variables involved in the persistence of overweight. The question as to whether a patient who remains overweight on ambulatory treatment should or should not be hospitalized can only be determined on the basis of the patient and not on the basis of a given amount of overweight per se. Overweight individuals adhering meticulously to a carefully planned and fully observed dietary regimen will lose weight unless there is an underlying metabolic or endocrine abnormality, emotional disorder, cardiovascular or renal problem, or deficiency disease. The persistence of overweight where an adequate reducing regimen has been outlined and strictly adhered to always merits further study to rule out functional or organic factors that may have been overlooked. Whether this should be through further study in the physician's office or through the medium of a period of hospitalization for additional diagnostic study and therapeutic supervision is a matter that can be determined solely on what seem to be the inherent needs in any given situation.

COIN LESIONS SHOWN IN CHEST FILMS

To the Editor:—*A routine chest film of a 60-year-old patient showed a coin lesion in the middle lobe of the right lung. There was no history of illness or undue exposure to tuberculosis. The Mantoux test was positive. All other laboratory work, including Papanicolaou's stain of sputum, was negative. All cultures and guinea pig tests were negative. Resection was done. The pathologist reported a "well encapsulated, calcerous mass measuring 1 cm. in diameter. The lining of cavity is granular. Section shows well demarcated tubercle surrounded by epitheloid lymphocytes and Langerhans' cells." The diagnosis was pulmonary tuberculosis. Cultures from the resected specimen were negative for acid-fast bacilli. No organisms were demonstrated. Is a diagnosis of tuberculosis justified in this patient? If not, what etiological agents could produce such a lesion?*

M.D., Louisiana.

Answer.—In this case the finding of "a well demarcated tubercle surrounded by epitheloid lymphocytes and Langerhans' cells" seems to justify a diagnosis of tuberculosis. On the other hand, that the tuberculosis is open and clinical seems problematical. This probably should be classified as closed, healed tuberculosis, and the patient should be considered well after removal of the lesion. It might be well to keep him on therapy with antituberculosis drugs for a number of months, as a precautionary measure. A good many of the coin lesions with calcification in them have been found to be caused by histoplasmosis, and differentiation between a nodule of this kind caused by tuberculosis and one caused by histoplasmosis is difficult. In the pathology department with which this consultant is familiar, these nodules are all called "granulomas" and are not said to be caused by either tuberculosis or histoplasmosis unless the sections show tubercle bacilli or the histoplasmosis organism.

VITAMIN A AND LOSS OF HAIR

To the Editor:—*Is there any evidence that taking large doses of vitamin A makes the hair fall out from the scalp, as stated in a syndicated newspaper article? If so, what is the dose of vitamin A that can be prescribed safely when such therapy is indicated?*

M.D., Connecticut.

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—Diffuse alopecia is sometimes associated with other frank signs of chronic or subacute hypervitaminosis A, such as hepatomegaly, fissuring of the corners of the mouth, and thickening and tenderness of the bone cortex in certain areas. Large doses of vitamin A (e. g., 5,000 to 50,000 I. U. daily) can be administered with safety for a week or 10 days in patients with signs of frank or latent deficiency. For ordinary prophylaxis, daily dosages should be limited to 3,000 I. U.

Answer.—The question regarding hypervitaminosis A and hair loss has a timely answer in a report by Elliott and Dryer in The Journal (161:1157 [July 21] 1956), where a case of hypervitaminosis A in an adult is reported. No hair loss was noted in this patient who received vitamin A in a dosage of 50,000 units three times a day for over seven months. This report also refers to other cases of hypervitaminosis A described in the literature where hair loss was noted along with symptoms referable to the bones and joints, notably bone tenderness, and skin changes. The dosage level of vitamin A that produces symptoms of hypervitaminosis A undoubtedly remains quite variable because of numerous factors subject to considerable biological variability.

MAINTAINING TISSUE TONE WHILE REDUCING

To the Editor:—*Would general body massage, done by a trained physiotherapist, be useful to maintain good tissue tonus in a patient who has been hospitalized to reduce his overweight of 50 lb. (22.7 kg.)? He has not yet developed signs or symptoms of additional disease. Are there any other benefits to "general body massage?" How often would it be recommended?* *Leonard Casser, M.D., Cresskill, N. J.*

Answer.—Opinion varies as to the extent of usefulness of massage in maintaining "tissue tonus" in a patient who has lost weight. Depending on the method of application and type of massage used, the psychic effect can be either a stimulative one or a sedative one. Blood flow to and from and lymph return from an area may be increased by the use of massage, and, secondary to this, a mild increase in metabolic activity may result. It is doubtful that massage alone can be expected to produce the desired effect in the patient who has lost weight. Probably more effective in bringing about this desired result would be the use of such active exercise as the patient's physical limitations permit. The benefits derived from carefully prescribed and graduated activity will undoubtedly exceed any of those derived from general body massage given every other day.

REMOVAL OF FLUORIDES FROM WATER

To the Editor:—*Will a water softener remove the fluoride compound such as is being used by the city of Chicago in their fluoridation program?* *John B. Jacobs, M.D., Chicago.*

Answer.—The ordinary household type of water softeners will not remove fluoride compounds from water. The commercial type of water softener known as a demineralizer will remove a major portion of the fluoride compounds added to water in fluoridation programs. These demineralizers will remove fluoride compounds so long as they are ionizable. Should a small amount of fluoride combine with organic (unionizable) compounds, these will not be removed.

ARTERIOSCLEROSIS AND DIET

To the Editor:—*A patient who eats cottage cheese twice daily rarely eats meat or fish. Would this be a good diet for one who has angina pectoris or arteriosclerotic heart disease? In other words does this kind of cheese produce too much cholesterol for such a patient? He adds moderate amounts of cream to the cheese.* *M.D., Indiana.*

Answer.—The diet outlined above is certainly not a desirable diet for a patient with atherosclerotic heart disease for several reasons. 1. It is necessarily too high in fats (including cholesterol and saturated fats). 2. Cottage cheese being the main source of protein, it is probably lacking some of the essential amino acids, vitamins, and minerals. This constitutes a dietary imbalance that, according to modern concepts regarding the pathogenesis of atherosclerosis, probably has deleterious effect on the vascular tree, particularly the coronary arteries. The patient should be advised to modify his dietary habits by substituting lean meats for at least part of his cottage cheese–cream intake. In general, a well-balanced diet deriving not more than 25 to 30% of the daily calories from fats and containing liberal amounts of fresh and cooked vegetables and whole grain products, is considered as optimal at present.

LACTATION IN INFANCY

To the Editor:—*A 10-month-old girl has milk in one breast. A small amount can be expressed on pressure. What, if anything, should be done? Is it likely to go away of itself?* *M.D., Virginia.*

Answer.—The presence of a small amount of thin milky secretion in the breast of an otherwise normal 10-month-old female infant has no significance. Spurious lactation in infancy is considered to result from stimulation of the breasts by maternal hormones that pass through the placenta to the infant during fetal life. The condition requires no treatment and can be expected to clear spontaneously if the breast is not irritated by tight clothing or manipulation.

BATHING NEWBORN INFANTS

To the Editor:—*Please review the current trend of thinking concerning the bathing of newborn infants with a mild soap and water as opposed to a method of oiling them with one of the acceptable baby oils. Various sources indicate that most of the larger obstetric hospitals have completely abandoned the use of oils.*

James M. Covington Jr., M.D., Wadesboro, N. C.

Answer.—Neither method is satisfactory. The current thought is best expressed by the Standards and Recommendations for Hospital Care of Newborn Infants (American Academy of Pediatrics, 610 Church St., Evanston, Ill., 1954), section 7, page 34: "No water or oil bath should be given during the hospital stay"; page 81: "Blood should be removed with cotton and water. Only unsightly amounts of vernix caseosa are to be removed. This should be done with sterile cotton. The skin thereafter should be left alone. Buttocks are to be cleaned with warm tap water with as little rubbing as possible. If needed, oil may be used over the diaper area."

RECURRENT BILIARY COLIC

To the Editor:—*A 50-year-old woman with a typical clinica history of recurrent biliary colic showed on three differen occasions a nonfilling gallbladder on Graham-Cole serie: There is no history of jaundice. At operation the gallbladd and biliary tree appear normal to visualization and palpatio The pancreas is apparently normal to palpation. What, if an procedures should be performed at the operating table?* *M.D., New York.*

Answer.—In the absence of objective evidence of disease the gallbladder at operation, cholecystectomy or cholecystostor should not be done. Careful exploration of the abdomen shou be made to exclude the possibility of chronic disease elsewhe The results after removal of a gallbladder that appears norn have not been good in a large proportion of patients. A hi incidence of biliary dyskinesia has been encountered. If syr toms persist after recovery from the operation, it might be w to place the patient on a low-residue, nonlaxative diet and administer belladonna and phenobarbital. In many patie hypermotility of the colon rather than disease of the gallblad is responsible for these symptoms.

PULLING TEETH DURING POLIOMYELITIS SEASON

To the Editor:—*The following quotation from the* Newsletter of the Medical Society of the State of New York *may be of interest in connection with the Query and Minor Note on "Pulling Teeth During Poliomyelitis Season" in* The Journal, *Sept. 29, 1956, page 527. "The State Health Department's recommendation that poliomyelitis vaccination continue during the summer does not apply to elective injections of other than polio vaccine. Probably a person who has received two or three injections of poliomyelitis vaccine faces little risk of getting paralytic polio even if the elective procedures are carried out in an area where the disease is prevalent. However, since the number of persons who have completed the course of three injections is still relatively small, the Department feels that the wisest course for this summer is to recommend postponement both of such elective injections and of elective nose, throat and mouth operations, especially in areas where polio is prevalent. Drs. Jonas Salk and David Bodian, with whom we have discussed the question, are in accord with this policy. As in the past, the avoidance of immunizations in infants under six months of age is not recommended since the hazard of polio is far less in this age group than the hazard of the other diseases against which infants are routinely immunized."*

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« Washington News »

State Officials Favor Vaccine Grants Extension • •
Democrats Set to Organize Committees Again • •
Casualty Care Program Undergoing Reevaluation • •
Cerebral Palsy Collaborative Study Launched • •
Military Surgeons Hear VA Research Potential • •

ENDORSEMENT OF HEALTH PROGRAMS BY STATE HEALTH OFFICIALS

Salk Vaccine.—The first public endorsement of extension of the Salk vaccine grants program for another year has been made by state and territorial health officers. This was one of the recommendations during their annual conference in Washington, D. C., with the surgeon general of the Public Health Service and the chief of the U. S. Children's Bureau. Without elaboration, the group voted that "the federal government should continue its financial participation in the poliomyelitis vaccine program for the next fiscal year."

Dr. Leroy Burney, PHS surgeon general, earlier in the session spoke at length on the poliomyelitis program, but he took no stand on whether it should be extended beyond next June 30. He noted that for the first time since the vaccine was introduced manufacturers report they have on hand more than 17,000,000 cc. cleared and undistributed. He estimated total cases of the disease by the end of this year will amount around 16,000, the lowest since 1947.

He said it would seem reasonable to assume that vaccination has played an important part in holding down incidence of paralytic poliomyelitis this year. With a good supply on hand he said that now is the time to protect the unprotected—infants and preschool children, elementary and high school children, college students and expectant mothers—and to complete the three-injection schedule.

Funds for Health.—State health officials also made the following recommendations: (1) extension of the Hill-Burton hospital construction program for another five years beyond June 30, 1958, with the full authorization of 210 million dollars for funds for both the basic and the clinic-nursing home programs; (2) an increase in funds for water pollution control construction grants, from the present 50 million dollars a year to 100 million dollars, and a total authorization of at least 1 billion dollars; similarly an increase in funds for air pollution control; (3) development by the PHS of legislation dealing specifically with the prevention and control of chronic disease and the promotion of the health of the aged, including a state grant-in-aid program; and (4) promotion by the PHS of a bill that would permit the PHS to cooperate with communities in construction of hospitals jointly serving Indians and non-Indians and that would make available to non-Indians space in existing Indian hospitals as well as medical services, subject to proper safeguards for rights of the Indians.

The Association of State and Territorial Health Officers meeting at the same time recommended that its president name a committee for long-range planning in public health, including promotion of legislation. The association elected these officers: Drs. Franklin D. Yoder, Wyoming state health officer, president; Herman Hilliboe, New York, vice-president; and Mack L. L. Shanholtz, Virginia, secretary-treasurer.

ELECTIONS AND HEALTH PROGRAMS

With at least another two years of coalition government ahead, the Democrats are set to organize the House and Senate again starting Jan. 3. Excepting the House Interstate and Foreign Commerce Committee, all committees concerned in varying degree with health matters will be headed by the same chairmen as in the 84th Congress. Rep. Oren Harris (D., Ark.) will assume the full chairmanship of the Interstate Committee in January, to replace Rep. Percy Priest (D., Tenn.) who died after the adjournment of the 84th Congress.

The elections brought the defeat of a veteran member of the House Armed Services Committee, Rep. Dewey Short (R., Mo.). He played a part in the last Congress in the bill commissioning osteopaths in the armed services. Returned to the Congress after a lapse of two years is Dr. Will Neal (R., W. Va.). This brings the total of physicians in the 85th Congress to five. The others are Drs. Ivor Fenton (R., Pa.), Antonio Fernos-Isern of Puerto Rico, Walter Judd (R., Minn.), Arthur Miller (R., Neb.), and Thomas Morgan (D., Pa.).

Chairmen of the committees important to the medical profession for the upcoming session include Senators Lister Hill of Alabama, Labor and Public Welfare; Richard Russell of Georgia, Armed Services; Harry Byrd of Virginia, Finance; Olin Johnston of South Carolina, Post Office and Civil Service; and John McClellan of Arkansas, Government Operations. Those in the House include Representatives Jere Cooper of Tennessee, Ways and Means; Carl Vinson of Georgia, Armed Services; Olin Teague of Texas, Veterans Affairs; Tom Murray of Tennessee, Post Office and Civil Service; and William Dawson of Illinois, Government Operations.

There is every reason to believe that with the President barred by constitutional amendment from a third term, Democrats in Congress will look carefully into any medical or other domestic bills proposed by the administration. At the same time Democrats may be expected to press for their own program with an eye on retaining control of Congress in 1958 and recapturing the presidency in 1960.

OSTEOPATHS IN THE ARMED FORCES

The Department of Defense has laid down the rules it will apply to commissioning of osteopaths as military medical officers, an authorization voted by the last Congress. To be eligible for a commission, an osteopath must meet the following requirements, among others: 1. He must be a graduate of a college of osteopathy "whose graduates are eligible for licensure to practice medicine or surgery in a majority of the states, and be licensed to practice medicine, surgery, or osteopathy in one of the states or territories of the United States." 2. He must be recommended by one of the three military surgeons general and "possess such qualifications as the secretary concerned may prescribe." 3. He must have completed (*a*) a minimum of three years of college work prior to entering college of osteopathy, (*b*) a four-year course with a degree of doctor of osteopathy from a school approved by the American Osteopathic Association, and (*c*) 12 months or more of internship or residency training approved by

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From the Washington Office of the American Medical Association.

the American Osteopathic Association. The regulations were signed by Dr. E. H. Cushing, deputy Assistant Secretary of Defense for health and medical matters.

CIVIL DEFENSE

The country's civil defense casualty care program is undergoing a reevaluation by a 10-man medical task force. The group will make recommendations for defining the broad scope of medical care in the event of enemy attack on the nation and also will review lists of civil defense medical supplies and equipment and their functional packaging. The Federal Civil Defense Administration explained that the reevaluation stems from two logistical field tests of the casualty care program that centered around the agency's 200-bed emergency hospital. The first test was staged by the 68th Medical Group at Fort George G. Meade, Md., last April, when over 400 simulated casualties were processed through the hospital. A second test was held in June at Fort Sam Houston, Texas, with the Brooke Army Medical Center and the Army Medical Service School staffs. A simulated bomb drop produced 823 casualties, who were processed through collection points, treatment centers, and an emergency hospital.

The agency found it would have to plan for a larger number of immediate casualties and provide care for a longer period after an attack than previously planned. Earlier assumptions of the FCDA were based on caring for casualties for a three-week period after an attack. The 10-man committee includes Col. Joseph R. Schaeffer, Walter Reed Army Research Institute; Dr. James B. Mason, American College of Surgeons; Dr. Harold C. Lueth, Chairman, American Medical Association Committee on Civil Defense; Dr. Max E. Lichter, member of the A. M. A. Committee; Dr. Max M. Van Sandt, director of the FCDA medical care division; Milton C. Skolaut, U. S. Clinical Center; Major Harriet C. Werley and Capt. Eveline C. Hughes, Walter Reed Research Institute staff; Ruth C. Smith, director of Nurses, Delaware County Hospital; and Margaret K. Schaefer, chief nurse, FCDA health office.

LONG-TERM RESEARCH

The Public Health Service has announced the start of a broad coordinated research program that will seek to identify factors responsible for cerebral palsy, mental retardation, blindness, and deafness. The collaborative study is expected to take 10 to 20 years to complete, and at its peak more than 6,000 persons will be studied annually. Data to be collected by some 10 participating medical institutions will include complete family history, pregnancy and prenatal histories, a detailed account of events at birth, and a complete physical and psychological history of each child during his initial stay at the hospital.

Infants who show signs of stress, defects in development, or neurological problems will be selected for follow-up and will receive periodic psychological and neurological examinations. The PHS expects that the studies will clarify the role of heredity, brain injury and brain hemorrhage, lack of oxygen, difficulty in breathing, prenatal and postnatal infections, and anemia of the newborn infant in the development of neurological disorders.

Awards of more than $700,000 for a four-year study in this field have been announced for Yale University School of Medicine and Brown University. Yale's grant for the first year is $107,799 and Brown's, $97,633. More than a million dollars a year will be awarded under the collaborative program that is being coordinated by the National Institute of Neurological Diseases and Blindness. The institute will analyze all data obtained from the participating medical centers.

The study at Yale will be under the general direction of Dr. Gilbert H. Glaser, associate professor of neurology, and the study at Brown, under Dr. Eric Denhoff, medical director of the Meeting Street School, institution for the crippled. Studies at Brown will be made through the Cerebral Palsy Clinic at Rhode Island Hospital and the Providence Lying-In Hospital.

RESEARCH BY THE VA

The Veterans Administration has a serious responsibility to carry out medical research in the disabilities and diseases of the aging veteran population, according to the deputy chief medical director of the VA. Dr. Roy A. Wolford, addressing the 63rd annual meeting of the Association of Military Surgeons of the United States, noted that diseases of older veterans are primarily of a chronic nature and usually require long-term hospitalization.

He stated: "There has been a significant increase in the number of veterans hospitalized with heart disease, respiratory difficulties and diseases of the blood vessels, cancer, diseases of the digestive and genito-urinary system, arthritis and other bone and joint disorders. Their great number provides the Veterans Administration an opportunity to investigate these diseases in order to be able to offer more effective methods of diagnosis, treatment and rehabilitation. Nowhere else in the world are found patients in all stages of these diseases in such large number or under conditions so suitable for clinical investigation as in Veterans Administration hospitals."

Col. Sheldon S. Brownton of the office of the Assistant Secretary of Defense for health and medical affairs outlined the Defense Department program for encouraging medical schools to include in their curriculums those phases of medicine encountered in disaster situations, both military and civilian. He said that the Public Health Service and the Federal Civil Defense Administration are now providing funds for this program along with the Defense Department.

The delegates to the meeting elected Col. Amos R. Koontz as president, and these vice-presidents: Col. Charles R. Mueller, Brig. Gen. H. H. Twitchell, Major Gen. Wallace H. Graham, Dr. John W. Cronin, and Major Gen. James P. Cooney.

PERSONNEL

Dr. Martha May Eliot is retiring at the end of this year as chief of the United States Children's Bureau, Department of Health, Education, and Welfare. Dr. Eliot, who has been chief of the bureau since 1951, will become professor of maternal and child health at Harvard University. . . . Forrest E. Linder, Ph.D., formerly with the United Nations Statistical Office, has been appointed director of the government's new program for annual surveys of illness and disability in the U. S. The program was authorized by the last Congress, and $700,000 is available this fiscal year. Dr. Linder, who received a doctor of philosophy degree from Iowa State University, was one-time deputy chief of the U. S. Office of Vital Statistics.

THE JOURNAL

of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 162, NO. 13 CHICAGO, ILLINOIS NOVEMBER 24, 1956

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IMMEDIATE MANAGEMENT OF THE INJURED URETER

Vincent J. O'Conor, M.D., Chicago

• *Serious injuries to the ureter have often resulted during trauma, such as stab and gunshot wounds, to the abdominal or pelvic organs, but they also occur occasionally during surgical procedures on neighboring structures, diagnostic procedures such as cystoscopy, and therapeutic procedures such as irradiation. Preoperative urographic study is important in planning the operative attack on certain abdominal, pelvic, and retroperitoneal spaces. Preoperative introduction of ureteral catheters should be utilized more frequently to facilitate identification of the ureters during difficult dissections. The unintended inclusion of a ureter in a ligature must be corrected promptly; the release of such a ligature is more readily accomplished by teamwork between the surgeon and the urologist. The possibility that a ureter has been injured should always be considered whenever oliguria or anuria is observed during the first eight hours after any surgical operation in the vicinity of the ureters. If evidence of injury or ligation is found, prompt repair, with provision for tissue drainage, is imperative.*

The ureter is frequently injured during surgical or urologic manipulative procedures. Gynecologic operations, such as hysterectomy, either vaginal or abdominal; the removal of the ovaries or fallopian tubes; excision of intraligamentous cysts or tumors; and vaginal repair for prolapse of the uterus, may be accompanied by ureteral injury. Operations on or within the abdomen, especially resections of the sigmoid and rectum; unusual conditions of the appendix, especially when retroperitoneal; the removal of atypical pancreatic and mesenteric cysts; and other less common procedures, are sometimes complicated by ureteral injury. Occasionally, a portion of the ureter, along with a segment of the bladder, is present in an inguinal hernial sac. In such a case, injury of the ureter may occur during surgical repair. In cystoscopic procedures, especially during ureteral manipulation of calculi, the ureter may be torn or perforated. Strictures of or kinks in the ureter, especially when long-standing ureteritis has been present, will present anatomic changes that predispose the ureter to injury by even the slightest trauma.

The most common ureteral injury brought about by the urologist is that due to perforation from the various instruments designed to facilitate the passage of ureteral calculi. Perforation of the ureter secondary to general body trauma is unusual. Injury due to external stab and gunshot wounds is seen in wartime but is uncommon in time of peace. After irradiation, the ureter may become necrotic and perforate into the surrounding tissues or into an adjacent viscus; but, more commonly, the wall becomes thickened and stenotic, and ureteral obstruction and hydronephrosis result. Ureteral injuries have become somewhat more frequent in recent years due to the increasing number of radical surgical procedures in the treatment of carcinoma of the lower part of the intestine, uterus, and pelvic adnexa. A marked increase in the number of injuries associated with cystoscopic procedures has been noted in the past 10 or 15 years.

The problems surrounding possible injury of the ureter are much more difficult and obviously more complicated for the abdominal surgeon and gynecologist than are those for the urologist. The latter is dealing directly with this structure and will be aware of the possibility of injury at all times. Failure to recognize the accident at the time of operation rules out the opportunity for immediate repair, and the most favorable time for repair of such ureteral damage is at the time of the mishap or as soon afterward as possible. The longer the situation exists unrecognized, the more difficult the anatomic correction and the more serious the complications.

Prevention of Ureteral Injury

Teamwork between the urologist and the gynecologist or abdominal surgeon will greatly lessen the number of surgical accidents to the ureter and bladder. While there is no single method that will insure prevention of these injuries—and it is obvious that they may be expected to occur even in the hands of the most experienced and capable physician—a preoperative knowledge of the anatomy and function of both kidneys and ureters is of great value to the surgeon.

From the Urologic Department of Chicago Wesley Memorial Hospital and Northwestern University Medical School.

Read before the Section on Surgery, General and Abdominal, at the 105th Annual Meeting of the American Medical Association, Chicago, June 13, 1956.

These can usually be demonstrated by a satisfactory excretion urographic study. If the information is incomplete, a retrograde study should be done. The careful surgeon will insist upon having these data before performing operative procedures that might be complicated by ureteral injuries.

Anomalies of the ureters and kidneys and possible distortions and deviations from their normal courses will be demonstrated by excretion or retrograde pyelograms. Renal fusion, renal ectopia, changes due to previous urinary infections, and the presence of cysts or tumors should be apparent before the surgical procedure. It is surely not too much to ask that an excretion urographic study be done prior to elective operative interventions of such magnitude that ureteral ligation or injury might result during a difficult dissection. So many lesions of the upper urinary tract are symptomless, or silent, that preoperative urograms should seem as important to the surgeon as do blood chemistry studies and other commonly applied laboratory procedures. Intestinal tumors occasionally involve the ureter by encirclement without localizing symptoms.

The urologist has, to a considerable degree, convinced the gynecologist and the abdominal surgeon of the value of use of the indwelling urethral catheter prior to and immediately after extensive operative procedures on the structures adjacent to the ureters and bladder. I urge the placing of indwelling ureteral catheters before the operation as well. Prior to the discovery of modern urinary antiseptics, there was some justification for feeling that the risk of setting up infection in the upper urinary tract might outweigh the help that the presence of these catheters might give in identifying the ureters more readily; however, this objection lacks validity today. It is true that the placing of catheters entails a cystoscopic procedure carried out by a well-trained person, who must see that the catheters are properly inserted and that they do not slip down during the operation. The latter can readily be effected by temporarily suturing the ureteral catheters to adhesive tape attached to the indwelling urethral catheter. It is true that occasions will occur where the ureters cannot be easily identified even with the catheters in place. However, in most of these instances the ureteral injury will become rapidly apparent by the appearance of the catheter during the course of the dissection. The objection that, by having catheters in place, the surgeon will be given a false sense of security against ureteral injury does not warrant serious consideration. I favor preoperative ureteral catheterization, and at Chicago Wesley Memorial Hospital there is an understanding that some member of the urologic service will be available for this purpose at all times.

Therefore, prevention of ureteral injury requires (1) recognition of the fact that such injuries can and will occur in the most experienced hands; (2) recognition that a knowledge of the relationship of the ureters to the abnormal structures that one is planning to remove should be obtained preoperatively by urography; and (3) recognition that the preoperative placing of ureteral and urethral catheters will assist the surgeon in avoiding a surgical accident to the ureter and bladder. The surgeon should be especially diligent in identifying the ureter (1) where it crosses the bifurcation of the iliac vessels; (2) in the ovarian fossae; and (3) where it passes behind the uterine artery. When the dissection is deep in the pelvis, he should at all times have in mind the location of the bladder wall and the intravesical portion of the ureter.

Most of the avoidable injuries to the ureter result from lack of vigilance in the placing of clamps and ligatures. Curiously enough, it seems that more ureteral and bladder injuries follow procedures where the dissection was reported as easy and satisfactory than where it was reported as difficult. In patients with extensive chronic inflammatory disease, large uterine or ovarian tumors, and infiltrating neoplasms of the colon, the surgeon will more often be accurately aware of the danger of ureteral injury and will go to greater pains in identifying the ureter in an early stage of the surgical dissection.

Treatment of Ureteral Injury

The immediate treatment of injury to the ureter (I am not taking into consideration delayed treatment) may be relatively simple or annoyingly complicated. When accidental ligation is recognized during operation, release of the ligation, with or without the passage of a ureteral catheter, will usually be adequate. If section of the ureter has occurred, one must accurately identify the proximal and distal segments and unite them, preferably over a catheter, by direct end-to-end anastomosis. Chromic absorbable surgical suture (0000) on an atraumatic needle is the suture of choice. Two or three mattress sutures suffice.

Since the immediate management of an injured ureter entails not only anatomic restoration but also insurance against urinary extravasation, the provision for adequate drainage, both intraureteral and alongside the ureter, must be of prime consideration. The introduction of a ureteral catheter by the cystoscopist while the surgeon is searching for or attempting repair of the severed ureter may be most helpful. Likewise, the point of catheter arrest in the case of ureteral ligation may quickly define the area to be examined by the operating surgeon. If the situation does not warrant prolonged search for the area of injury or if repair is too difficult or considered unsatisfactory, nephrostomy should be performed after the abdominal wound has been closed, with provision for adequate drainage. It is well known that complete, sudden, simple ligation of the ureter is usually followed by an asymptomatic renal atrophy preceded by a complete unilateral renal suppression. All too often the surgeon may be tempted to follow this easy path out of the difficulty of unilateral ureteral injury. However, this would be most unwise unless previous renal functional and urographic tests had demonstrated a normal kidney on the unaffected side. Even then one would recommend nephrostomy reluctantly, except in the unusual instance where later surgical procedures or complications might outweigh the loss of function of one kidney.

Releasing of ligation should always be seriously considered when complete anuria has been shown by cystoscopic examination to be due to bilateral ureteral occlusion. In the past, there has been a high mortality from this secondary operative procedure; and the surgeon has, therefore, preferred to perform a bilateral nephrostomy or pyelotomy. The release of a ligation can be greatly simplified if the surgeon and urologist cooperate in its performance. The surgeon reopens the laparotomy wound and, with the aid of the cystoscopist, can readily detect the points of constriction when the ureteral catheters (preferably 7 to 9 F. in size) are used to prod the area of obstruction. After release of a ligation, the catheters should be passed to the renal pelves and left in place for from 5 to 10 days. Without the help of the urologist, the surgeon may conduct a prolonged search for the areas of ligation, remove the wrong sutures, and generally grope in the edematous tissue without finding the offending ligatures.

In my experience, the most satisfactory manner of handling the problem of intraureteral drainage is to have the surgeon insert a 6 to 9 F. ureteral catheter, either woven, latex rubber or polyethylene, so that one end is in the renal pelvis and the other end coils up in the bladder. The latter end is then grasped with a forceps or cystoscopic rongeur and pulled out through the urethra. An indwelling urethral catheter should be placed in the bladder and the ureteral catheter fastened securely to it to prevent its slipping down the ureter into the bladder. If the ureter has been injured low in the pelvic portion, within 3 to 5 cm. of the bladder, reimplantation of the proximal portion to the bladder should be effected, using either the pull-through-and-suture technique or the eliptical anastomosis with mucosa-to-mucosa suture as described by Nesbit. When irreparable injury has occurred in the lower half of the ureter, one can either transplant it to the sigmoid or, if possible, effect a ureteroureterostomy. I have never performed the latter procedure, but it has been carried out successfully by Higgins, Parke Smith, and others.

Prevalence of Ureteral Injuries

Any patient who shows oliguria or complete anuria during the first eight hours after operation should be suspected of having ureteral injury or ligation, if the surgical procedure has involved the region of the ureters. In unilateral occlusion, there may often be no symptom whatever, but partial anuria, pain in the flank or abdomen, and elevated temperature may suggest the condition.

Ureteral injuries from perforation during the cystoscopic extraction of calculi from the lower part of the ureter have increased materially in recent years. Mechanical stone extractors are usually the instrument of injury. At the time of extraction, the ureter may be more vulnerable to puncture because of the inflammatory or necrotizing action of a long-impacted calculus. Ureteral injuries occurring as a result of cystoscopic procedures and those associated with external trauma, such as gunshot and stab wounds, make up a chapter too vast to consider here. Rusche and Hager have completed a comprehensive study of 103 ureteral injuries encountered by them during the years 1930 to 1950. The increase in ureteral injuries after cystoscopic attempts at ureteral stone extraction was emphasized, as were such injuries due to gunshot wounds. They felt that, despite the increase in the number of patients subjected to extensive radical pelvic and abdominal surgery, a comparison of the period 1940-1950 with the preceding decade indicated that the number of surgical injuries remained about the same.

Summary

The gynecologist, general surgeon, and urologist must constantly bear in mind the possibility of ureteral injury during operative procedures in the abdomen, pelvis, and retroperitoneal spaces. Preoperative excretion urographic studies are most important in considering the operative attack. Preoperative introduction of ureteral catheters should be utilized more frequently to assist the surgeon in more readily identifying the ureter. These catheters should be fastened to the indwelling urethral catheter. The release of a ligation is more readily accomplished by teamwork between the surgeon and urologist. Early surgical repair, with adequate provision for tissue drainage, is paramount after injury or ligation has been discovered.

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PRIMARY CARE OF THE URINARY TRACT IN SPINAL CORD INJURY

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• *The structural changes that follow retention of urine in a paralyzed bladder must be prevented by adequate drainage from the beginning. With a catheter in place, the bladder regains its ability to fill and empty by reflex action with a certain regularity. It can be conditioned by the method of tidal drainage within a period of 6 to 12 weeks. Meanwhile a program of high fluid intake, acidulation of the urine, and muscular exercise is carried out to prevent lithiasis. The catheter can then be removed, and the observance of a certain program of fluid intake and other habits enable many patients to maintain an adequate urinary capacity, to empty the bladder completely, and to get along without wearing any apparatus.*

The management of the bladder in patients with spinal injury or disease has two aims: to provide the patient with a micturitional function that will not impede his efforts toward rehabilitation and to preserve the integrity and function of the upper urinary tract. Fortunately, these aims are not incompatible; indeed, the best assurance of a healthy upper urinary tract is a normally functioning bladder. If this can be achieved and if, at the same time, the hazard of formation of renal calculi because of disturbed calcium

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metabolism can be obviated, the disastrous train of events that has in the past led so many of these patients to invalidism and death may be averted.

There are two principles upon which the course of management that meets these demands is based. First, any functional disturbance, such as that caused by impaired innervation, will eventually result in reciprocal structural alteration; furthermore, if the dysfunction leads to secondary consequences, such as infection, secondary changes will develop and may become so marked that, even if the innervation were to be restored, the end-organ might remain incapable of normal activity. The object, therefore, is to prevent the development of such changes, to recognize them if they have already developed when the patient is first seen, to evaluate their contribution to the dysfunction, and, finally, to treat them if possible. The other basic principle is that the bladder is a spinal reflex organ with an overlay of controls from higher centers. Primary neurogenic dysfunction may result from involvement of the spinal center itself or from interruption of the pathways through which it communicates with the brain.

To guard against structural alteration, one must insure adequate drainage from the beginning. Overdistention leads to changes in the bladder wall; these are hastened by infection, which soon develops. Even when the patient can void, if there is residual urine (which is often the case), infection will follow. Catheterization is not without its risks and inconveniences, but these add up to a good deal less than the danger of infection in an inadequately drained urinary tract. Furthermore, by preserving the structural integrity of the bladder, early drainage hastens the day when, the process of retraining having been completed, artificial drainage may be discontinued and the patient may void naturally through the urethra.

Having secured the advantages of early drainage, one may expect that, as the patient emerges from the period of spinal shock and as the reflex activity below the level of the lesion is resumed, the bladder, although deprived of its controls from higher centers, will fill and empty reflexly with some degree of rhythmical regularity. This is the so-called automatic bladder; but the term is a bad one, and the function represented is not satisfactory. Such a bladder tends to be hypertonic; its emptying contractions are inefficient, and, as a result, it accumulates a considerable amount of residual urine. There is, of course, no control of micturition. In the name of expediency, treatment has often taken the form of permanent suprapubic drainage, permanent urethral catheterization, or the wearing of some cumbersome type of incontinence apparatus. Most of these undesirable eventualities can be avoided.

The Reflex Bladder

Management is based upon the fact that reflex activity of any kind can be conditioned to greater consistency and efficiency. Tidal drainage provides a method of applying this conditioning process and achieving that degree of consistency and efficiency that is the primary requisite of good function. If the patient is seen early, before any complicating factors have developed, this can be accomplished in an amazingly short time, perhaps as little as six weeks. It should seldom require more than three months. The catheter may then be removed and, by combining a controlled fluid intake with careful habit training, the patient may maintain an adequate capacity, empty his bladder completely, and have reasonably good control, so that it is unnecessary for him to wear any apparatus. It should be possible to achieve and maintain such a result in at least two-thirds of all patients. The program for prevention of calculi is simple but effective. It includes a high fluid intake (3,500 to 4,000 cc. daily), acidulation of the urine, muscular activity to avoid the mobilization of calcium from the skeleton, and adequate drainage. On such a regimen, the incidence of primary renal calculus should be less than 2%. The weeks immediately after injury are most critical.

This is not the time to discuss the exact techniques employed in the routine urologic care of these patients, such as the conditioning of the reflex bladder, the details of habit training, the indications for nerve blocks or nerve interruptions in special cases—and I should like to emphasize that these seem to me to be indicated only in special cases—and the indications for and technique of transurethral resection, which, in my experience, has been necessary in perhaps one out of every four patients. It should be remembered that there is no place for mere expediency in the attack on this problem. Nothing but the best will do if the two aims mentioned earlier are to be achieved. If they are not, the patient cannot anticipate a successful rehabilitation and probably will not live very long; he will certainly not enjoy good health.

Comment

It is only fair to point out, however, that this method of treatment is not easy to follow. It requires meticulous daily attention to detail and seemingly endless explanations to patients, nurses, attendants, and, in particular, to other doctors who are concerned in the patient's care. Above all, it demands the understanding and the willing cooperation of the patient, particularly during the difficult weeks of habit training shortly after the removal of the catheter. There is no way of avoiding this if the best results are to be obtained; I am not aware of any short cuts. The various surgical procedures that have at one time or another been suggested (some of which still have a useful place) are not substitutes for the fundamental program of conditioning of the reflex bladder but rather are supplements to it, to be employed when and if they are required, according to the needs of the individual patient. The other expedients to which I have referred briefly are easier for the doctor and make fewer demands upon the patient's understanding and cooperation. The only thing to be said for the more difficult approach recommended here is that it gives the majority of patients a much healthier urinary tract and keeps them alive and well longer.

NEUROSURGICAL ASPECTS OF TREATMENT FOR PATIENTS WITH SPINAL CORD INJURIES

Irving S. Cooper, M.D., New York

• *The first decision for the neurosurgeon after an injury to the spinal cord is whether any immediate neurosurgical maneuver is indicated. Neurological and roentgenographic examination determine whether fracture-dislocations need to be reduced, whether traction or laminectomy are necessary, and whether post-traumatic fragments of bone, intraspinal hematomas, or herniated intervertebral disks require attention. In many cases early laminectomy is actually the conservative course of action. Later problems for the neurosurgeon, from three months to several years after the injury, concern especially the intractable pain and spasticity that generally accompany paraplegia. Various procedures, including chordotomy, offer reasonable hope of relief of pain; alleviation of spasticity may be afforded by peripheral neurectomy, subarachnoid alcohol block, rhizotomy, or subtotal spinal chordectomy.*

Since I shall discuss only the aspects of the care of patients with spinal cord injuries that are directly related to neurosurgical management, it will be necessary to integrate these remarks with those of the other speakers on the panel (this issue, pages 1203-1204 and 1208-1209) in order to arrive at an over-all picture of management for patients with spinal cord injuries. As Dr. Covalt has stressed, the patient with spinal cord injuries should be taken directly to the x-ray department so that roentgenograms might be obtained without any additional moving of the patient. It is at this point, while the patient is still in the x-ray department, that a decision should be made as to whether neurosurgical care is immediately indicated, assuming that the neurosurgical consultant has been called to see the patient. After a detailed neurological examination and appraisal of the roentgenograms, the first decision that the neurosurgeon is called upon to make is whether any immediate neurosurgical maneuver is indicated.

Early Neurosurgical Treatment

In cases of fracture-dislocation of the cervical spine in which reduction must be carried out, this is usually performed properly by skeletal traction applied to the skull. The method that is commonly used is the application of Crutchfield tongs to the crown of the skull or wires passed through trephine openings in the skull. Thus, in a great majority of cases of fracture-dislocation of the cervical spine, proper reduction with decompression of the spinal cord, which is the initial treatment of choice, can be accomplished by skull traction. In cases in which skeletal traction properly applied has not been able to reduce the dislocation or in which a subarachnoid block persists despite adequate use of traction, cervical laminectomy with decompression is indicated. Another indication for open operation is progressive increase in neurological deficit despite satisfactory skeletal traction. In some instances of violent injury to the cervical portion of the spinal cord, acute herniation of the intervertebral disk also occurs. Usually, clinical and roentgenographic studies will aid in the diagnosis of this lesion, although occasionally myelography is necessary. In such instances, laminectomy with decompression of the spinal cord should be performed.

In cases of thoracic and lumbar fracture-dislocation, the subject of laminectomy versus more conservative management continues to be controversial, although an increasing number of neurosurgeons now seem to feel that laminectomy and decompression is the treatment of choice in almost every case. It has been my own policy to recommend that laminectomy be performed early in every case of paraplegia that is caused by injury of the thoracic and lumbar spine. It is my opinion that early, routine laminectomy in such cases is actually the conservative course of action and that it can be done safely and without causing any delay in the ultimate rehabilitation of the patient.

There are many reasons why laminectomy should be performed, some of which have already been enumerated in early reports. Very briefly, some of the reasons for laminectomy are as follows: 1. In the thoracic and lumbar region it is an operation that can be performed quickly, under local anesthesia if necessary, without interfering with the stability of the spinal column and with a mortality rate that is practically nil. 2. There is no way during the immediate post-traumatic period in patients demonstrating complete paraplegia to ascertain, by either neurological examination or roentgenographic examination, whether there has been an anatomic transection of the spinal cord. An examiner is not justified by either clinical examination or roentgenologic examination in concluding that the spinal cord has been irreparably damaged. The only way one can determine early, in patients demonstrating complete loss of motor and sensory function, whether the spinal cord is anatomically transected is by direct exploration. Therefore, the patient should not be denied laminectomy because the examiner has the impression that the spinal cord is already hopelessly injured. 3. It can be considered that in some cases the removal of depressed laminas and other post-traumatic fragments of bone as well as intraspinal hematomas may have a beneficial effect upon future spinal cord function. 4. Wide débridement with intradural exploration may help to prevent late arachnoiditis and other later complications, such as pain and spasticity. 5. If wide decompression of the injured area of the spinal cord is performed shortly after injury, early mobilization and rehabilita-

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Read in the Panel Discussion on Rehabilitation of Patients with Paraplegia before the Section on Physical Medicine at the 105th Annual Meeting of the American Medical Association, Chicago, June 12, 1956.

tion may be instituted more safely than if the patient still has spinal cord compression. 6. Paraplegic patients logically conclude that direct exploration and decompression of the spinal cord should be attempted, if there is not some definite medical contraindication, before they are asked to resign themselves to a lifetime of paraplegia and a long period of rehabilitation for their paralyzed extremities.

Alleviation of Sequelae

During the late phases of care for the patient with spinal cord injuries, that is, from three months to several years after injury, the neurosurgeon may be able to play a role in alleviating some of the undesirable sequelae of paraplegia. For the purpose of this discussion, I shall limit myself to two of the most intractable and distressing complications of spinal cord injury, pain and spasticity. Although these phenomena are not both invariably present in the same patient, there is some justification for considering pain and spasticity simultaneously. Both of these phenomena are paradoxical neurological sequelae of spinal cord injury. In the case of pain, this sensation is usually referred to areas rendered anesthetic and analgesic by the spinal cord lesion, so that heightened pain sensation is present in an area from which the application of painful stimuli cannot be appreciated. Likewise, spasticity in patients with paraplegia reflects exaggerated involuntary motion of muscles that cannot be moved voluntarily. Thus, these phenomena, namely, pain referred to analgesic areas and exaggerated activity in paralyzed muscles, are considered to be physiologically related. Moreover, in evaluating the etiology of these distressing sequelae, there is considerable evidence that not only the destructive elements of traumatic lesions but also the irritative effects of such injuries must be taken into account. For these reasons, pain and spasticity may be considered together.

Management of Pain.—Approximately 75% of the patients who incur spinal cord injury will, at some time during their course, complain of some type of severe pain. Because of the nature of such an injury, which may render a large part of the body numb, pain in these patients is particularly difficult to evaluate. No single classification of pain in paraplegic patients has been suggested that can be considered inclusive. Moreover, an etiological classification is not feasible at this time, inasmuch as the individual roles of the sympathetic nervous system, spinothalamic tract systems, and unrelated pathways have not yet been elucidated in these cases. Since there are some obvious differences in the mechanisms productive of pain during the early weeks after injury and those productive of pain after this period, it is well to consider pain early and late after spinal cord trauma.

Early Pain: A surprisingly small percentage of patients complain of severe pain over the site of vertebral injury. Many vertebral fracture-dislocations are unattended by local pain. In my experience, local discomfort is more common in cases of cervical fracture-dislocation than in fractures in other regions of the vertebral column. The treatment dictated by consideration of spinal cord lesion, as outlined earlier (that is, early skeletal traction in cases of cervical lesions and early laminectomy in cases of thoracic or lumbosacral lesions), will invariably alleviate the pain produced by the bony abnormality. In the cases in which spinal fusion is indicated, this procedure will also lessen the likelihood of prolonged local pain. Consequently, local pain over the site of vertebral fracture seldom becomes intractable and is usually managed without difficulty.

The two common neurological causes of pain in the nerve root are cartilaginous compression and complete intraspinal subarachnoid block. The presence of a complete subarachnoid block, particularly in the lower thoracic or lumbar region, will often produce severe pain in both lower extremities. This pain is often sharp and lancinating in character, as well as constant and excruciating. It may be diffuse throughout the extremities. It is sometimes accompanied by burning paresthesias. The pain is aggravated by extension of the back, coughing, sneezing, or other activities that tend to increase intra-abdominal and thus intraspinal pressure. Roentgenologic examination may provide evidence of narrowing of the intraspinal canal, and the presence of a subarachnoid block is confirmed by spinal puncture with careful manometric studies. Once this block is demonstrated, early laminectomy with decompression of the block is indicated. Surgical decompression will usually result in prompt relief of pain due to this cause. Since the presence of an intraspinal block is in itself indication for laminectomy, further discussion of pain due to such a cause is not necessary.

Pain due to compression of one or more nerve roots even in the absence of an intraspinal block is not infrequent in cases of vertebral fracture-dislocation. Compression of such roots may be due to anterior dislocation of a fractured lamina, posterior dislocation of part or all of the body of a fractured vertebra, protrusion of bony fragments into an intervertebral foramen, or traumatic protrusion of an intervertebral disk. The occurrence of the latter phenomenon is more common than had formerly been thought and has been emphasized recently, particularly as a cause of neurological damage in the cervical region.

Radicular pain due to one of the afore-mentioned causes of nerve root compression is recognized by those qualities peculiar to root pain: 1. The pain follows the anatomic distribution of one or more nerve roots. 2. Paresthesias along the same distribution are not uncommon, particularly in cases of incomplete transection of the spinal cord. 3. The pain is aggravated by coughing, sneezing, or straining. 4. The pain is usually intensified at night after the patient has been in an extended or hyperextended posture for some time. 5. The pain is usually sharp and lancinating in character.

Careful neurological evaluation and roentgenologic study will usually indicate the site at which radicular compression is occurring. Roentgenographic demonstration of a fracture extending through one of the intervertebral foramens, an extreme narrowing of an intervertebral disk space, or an obvious bony abnormality may indicate the vertebral site of nerve root compression. In some instances, in the absence of such roentgenologic findings and in the absence of a subarachnoid block, contrast myelography may be utilized as an adjunctive aid in evaluating the site and cause of nerve root compression following spinal injury. However, this latter procedure is to be avoided in such cases whenever possible. Many spinal cord injuries are accompanied by subarachnoid or intramedullary hemorrhages, arachnoidal lacerations, and other types of lesions conducive to fibroblastic reaction. Superimposed upon such a nidus, the introduction of iodized oil (Lipiodol) or iophendylate (Pantopaque) may contribute to the development of an adhesive arachnoiditis. This is a common finding in cases in which exploration is done one or more years after injury, and such arachnoiditis is undoubtedly a contributing factor in production of the sequelae of spinal cord trauma.

Surgical exploration and decompression is the treatment of choice in cases of pain due to nerve root compression. Hemilaminectomy, foraminotomy, or removal of a protruded intervertebral disk, depending upon whichever proves to be indicated, will often relieve radicular pain. Treatment of this type of injury to the spinal cord or cauda equina will be more successful in those cases in which decompression is carried out early, before the pain has become constant and before the patient has become dependent on narcotics.

One other cause of pain in paraplegic patients during the early days following spinal cord injury is the presence of concomitant injuries to other body parts, such as a ruptured spleen or traumatic hemothorax. Such a category is too obvious to require further elaboration and is mentioned only for the sake of completeness. However, I have seen patients in whom extraspinal injuries had been overlooked because of the initial examiner's preoccupation with the major symptom of paraplegia. Vigilance in a complete physical examination obviates such errors.

Late Pain: Pain of an intractable nature is more often a complaint of the patient three or more months after injury than during the early post-traumatic period. This pain has been classified by several authors. Most writers seem agreed that pain in the lower extremities may be of an intermittent, sharp, lancinating, radicular quality; a diffuse, dull aching quality; or a burning causalgia-like quality. The first type is most frequently seen in cases of injury to the cauda equina, while the second type is more commonly encountered in injuries of the spinal cord proper. The diffuse burning type of pain may be present in cases of injury to either the spinal cord or the cauda equina. Although the burning pain complained of by persons with paraplegia is similar to that usually described as causalgic, this type of pain in paraplegic patients is seldom, if ever, entirely relieved by sympathectomy. Holmes postulated that such persistent burning pain might be due to changes in the anterolateral columns of the spinal cord. Förster's investigations demonstrating that the entire pain pathway in the spinal cord is excitable substantiated Holmes' hypothesis. This still offers the best physiological explanation for the presence of diffuse aching, burning, tingling, or other nonradicular pains of the insensitive lower extremities of the paraplegic patient.

It has been my experience that all the categories of pain described in the preceding paragraph (that is, the radicular type of lancinating pains; diffuse, deep aching pain; or constant burning, tingling pains occurring in the insensitive paralyzed lower extremities), present three months or later after spinal cord injury, are best treated by bilateral high thoracic or cervical spinothalamic chordotomy. Like most neurosurgeons, I have had disappointing results with the use of spinothalamic chordotomy for pain in some paraplegic patients. However, if patients are selected who have not yet become addicted to narcotics and whose pain is not psychologically motivated, and if such patients are operated on under local anesthesia to allow instant appraisal of the level of analgesia achieved, the incidence of successful relief of pain will be reasonably satisfactory.

Relief of Spasticity.—In persons with traumatic paraplegia, spasticity of the paralyzed lower extremities becomes marked enough to impede rehabilitative measures in approximately 40% of those with injuries to the cervical and thoracic portions of the spinal cord. The relief of this spasticity will often enable a bedridden paraplegic patient to become ambulatory and self-sufficient. The four types of neurosurgical procedures that will alleviate intractable spasticity in the paraplegic patient are as follows: (1) peripheral neurectomy, (2) subarachnoid alcohol block, (3) rhizotomy, and (4) subtotal spinal chordectomy.

Peripheral Neurectomy: The resection of peripheral nerves has rather limited usefulness in relief of spasticity in paraplegic patients. It is confined largely to resection of the obturator nerves for relief of adductor, or scissors, spasticity. When the incapacitating spasticity is largely confined to the adductor muscles of the thighs, the procedure of choice is bilateral transabdominal obturator neurectomy. This procedure can be performed easily and provides immediate relief. The nerve is approached retroperitoneally through a McBurney abdominal incision and is readily identified as it emerges from the medial side of the psoas muscle to cross the brim of the pelvis. Stimulation of the nerve to produce adduction of the thighs positively identifies it prior to resection.

Subarachnoid Alcohol Block: Subarachnoid alcohol block has emerged as the single most useful and most applicable method available for relief of paraplegic spasticity. The indications for subarachnoid alcohol injection are essentially those previously applied to anterior rhizotomy. The chief indication is intractable spasticity of the lower extremities, which have no useful motor or sensory function. Enough time should have elapsed from the time of injury so that the lesion may be known to be stationary; this eliminates the possibility of future neurological recovery. This procedure has certain advantages over anterior rhizotomy: it is safer and more easily performed and is free of the hazards of major surgical procedure. Its effects are immediate and, in most instances, of long duration. It is, however, not selective. Thus, if certain nerve roots, such as those to the detrusor urinae, are to be excluded, this method is contraindicated in favor of selective anterior rhizotomy. Such contraindications, however, are rare, particularly since it has been demonstrated that satisfactory autonomic micturition and sexual potency in the male can develop after subarachnoid alcohol injection.

The technique of subarachnoid injection I now use is as follows: The patient is placed on his side in bed, and the foot of the bed is elevated 18 in. An 18-gauge spinal puncture needle is inserted at the first lumbar interspace. A syringe containing 15 cc. of dehydrated alcohol is attached to the needle, and the alcohol is injected at the rate of 1 cc. every 15 seconds. An assistant constantly checks the patient's vital signs and the level of anesthesia during the injection. The injection is continued until both legs have become completely flaccid or until 15 cc. of alcohol has been injected. The patient is then turned on his back and kept in this position for four to six hours. He is allowed out of bed on the following day. If the injection has not produced satisfactory flaccidity, it is repeated the following day, with an additional 10 cc. of alcohol being used.

Rhizotomy: Rhizotomy, or intraspinal resection of nerve roots, is the time-honored method of relieving paraplegic spasticity, used since the introduction by Förster of posterior root section for spastic paraplegia. The fact that posterior rhizotomy alone did not provide adequate relief of spasticity led Munro to develop the technique of anterior dorsolumbar rhizotomy. This method requires laminectomy and division of all anterior nerve roots from the 10th thoracic through the 1st or 2nd sacral. The last firm dentate ligament is usually regarded as indicating the level of the first lumbar nerve root, although this relation is not invariable. If one is anxious to avoid sacrificing the motor supply of the detrusor urinae (usually the second and third sacral roots), these roots can be positively identified by stimulating each sacral root individually and at the same time recording the intravesicular pressure. Unless one is desirous of sparing certain nerve roots, such as those which innervate the urinary bladder, or unless some sensation exists in the lower extremities, subarachnoid alcohol injection is probably to be preferred to anterior rhizotomy.

Subtotal Spinal Chordectomy: Occasionally one is faced with the problem of recurrent spasticity after subarachnoid alcohol injection. In these circumstances the operation of anterior rhizotomy is made very difficult by the dense adhesive arachnoiditis produced by the prior alcohol injection. This arachnoiditis usually makes positive identification of individual roots impossible. In such cases, one may resort to subtotal resection of the spinal cord. This subtotal chordectomy involves resection of the spinal cord and nerve roots below the level of the 9th or 10th thoracic segment. The operation requires a laminectomy extending from the 9th or 10th thoracic to the first lumbar level and is performed more quickly and easily than is anterior dorsolumbar rhizotomy. McCarty has demonstrated that removal of the entire cord in man below the second thoracic level is not incompatible with life. In my experience, removal of that section of the spinal cord below the ninth thoracic level has had no untoward or unexpected sequelae.

Summary

During the early management of the patient with spinal cord injury, the neurosurgeon may contribute to the neurological evaluation. He may perform skeletal reduction of cervical fracture-dislocation and laminectomy as well as decompressive procedures when these are indicated. The principal sequelae that often require the attention of neurosurgeons during the later phase of this problem are intractable pain and spasticity. There are various neurosurgical methods that may be utilized in the management of these sequelae.

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REHABILITATION OF THE PARAPLEGIC PATIENT

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• *The end-result in rehabilitating the paraplegic patient is preparing him for a job, or at least preparing him for further vocational training that will result in a job. Total rehabilitation requires the cooperative services of the neurosurgeon, urologist, orthopedic surgeon, and physiatrist. The series of activities presented, which follow definitive care, are directed to the paraplegic patient's adjustment to walking and daily living.*

The rehabilitation of the paraplegic patient can only be accomplished with the closely knit cooperation of the neurosurgeon, urologist, orthopedic surgeon, and physiatrist. On admission, the patient should be taken directly to the x-ray room so that the neurosurgeon, having been called in to see him, can decide upon the advisability of surgery. The physiatrist should be called early to see the patient, who should be put on a Stryker frame or sponge-rubber mattress and turned every two hours. Particular attention should be paid to the skin over the sacrum and over the knees, as well as to that over the ischial tuberosities and the two trochanters. These areas should be cleansed carefully, massaged lightly, and oiled with some bland ointment or oil each time the patient is

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Read in the Panel Discussion on Rehabilitation of Patients with Paraplegia before the Section on Physical Medicine at the 105th Annual Meeting of the American Medical Association, Chicago, June 12, 1956.

turned. It is important that the patient be placed in a neutral anatomic position, and, if necessary, splints should be put on to preserve the right angle of the foot on the ankle.

The physical therapist should be given instructions about exercising the joints of the patient's paralyzed extremities through a complete range of motion. Also, the patient should be given exercise for stretching the Achilles tendon. While the patient is in bed, either waiting for a laminectomy or recuperating from the operation, he should be given exercises to strengthen the muscles of the upper extremities. These are the muscles that will help him to walk after he is given braces. Particular attention should be paid to the triceps and latissimus dorsi muscles

I do not recommend use of the triangular overhead bar, as some do, to aid patients in pulling themselves up into a sitting position, the patient only needs enough strength in the biceps to feed himself. Therefore, our patients are instructed to push themselves up with their hands placed behind them. This utilizes the triceps muscles and enables the patient to gain a sitting position. As soon as clearance is obtained from his neurosurgeon and/or orthopedic surgeon, the patient should be placed on a tilted board, with straps over his chest, hips, and knees, and should be allowed to stand in a vertical position. To start with, he should be allowed to stand at an angle of 25 to 30 degrees and only for a few minutes. This should be gradually increased, so that at the end of two weeks he should be standing in a vertical position for at least one hour a day. We know from research work that has been done[1] that an hour of standing a day will keep the calcium in the long bones of the legs and help to prevent urinary calculi and infection, which is the killer of paraplegic patients.

Braces should be ordered as soon as possible. We use as a rule of the thumb the 10th thoracic vertebra as a starting point. Those patients with lesions at T-10 and above are usually given double bar long braces with pelvic band and Knight spinal attachment for the back; those with lesions from T-10 to L-1 are given double bar long leg braces with pelvic band; and those with lesions below L-1, depending upon the musculature present, are given long leg braces.

Walking and Daily Living

The patient is brought to a standing position in the parallel bars and is usually started out with a "drag to" gait; he then advances to a "swing to" gait and, finally, a "swing through" gait. As soon as he is proficient in the parallel bars, the bars are eliminated and he is given crutches and taught to ambulate, at first with assistance and later by himself. The patient must be taught to climb curbs. We usually start with a 2-in. curb and graduate to a 4-in. curb and, finally, a 6-in. curb. Next, the patient must be taught to climb stairs. This is ordinarily taught with a one-hand rail and one crutch, the patient being allowed to carry the other crutch.

Also, the patient must be given an intensive course in activities of daily living. This would include training in transfer activities such as those from the bed to the wheelchair and back again, from the wheelchair to the toilet and back again, and from the wheelchair to a standing position and back again. He must be taught how to dress himself as well as all personal hygiene activities. Last, but not least, the patient must be taught to drive his own car, utilizing some of the simple hand-control devices that can be installed very inexpensively. Bowel and bladder training is most important. Bowel function is controlled by means of careful diet and the use of glycerin suppositories every other day. The majority of our patients do develop an automatic bladder control. However, since many of these patients return to active lives, they must be protected by some type of rubber urinal.

While the paraplegic patient is finishing his physical restoration, it is important that vocational possibilities be explored. In that way, when the patient is ready to leave the rehabilitation center he will know that he is prepared either to go to a job or to take further vocational training that will result in a job.

Summary

The patient with paraplegia should be kept on an active rehabilitation program from the time he is admitted to the hospital until he is discharged. He should be taught to become as self-sufficient as possible. Vocational possibilities should be explored, so that he may return to a job as soon as possible or may go on to further vocational training. Early rehabilitation procedures help to prevent the complications to which these patients are so liable. Later, the program must become more active and should include training in ambulation with braces, wheelchair activities, and hyperdevelopment of the patient's remaining muscles.

400 E. 34th St. (16).

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Capillary Thrombosis.—Capillary thrombosis is observed in a number of conditions. Extensive involvement has been reported in a variety of diseases, such as rickettsial infections, disseminated lupus erythematosus, periarteritis nodosa, malignancy, aplastic anemia, and thrombotic thrombocytopenic purpura. The pathogenesis is as yet undetermined. Moschcowitz was the first to report an instance of thrombotic thrombocytopenic purpura, this he did in 1925. He believed the thrombi consist of agglutinated erythrocytes, and pointed out that there is no evidence of primary vascular disease. Altschule ascribed the lesions to damage to the vascular endothelium, with secondary deposition of platelets. Muirhead and associates reported one case in which there were extensive endothelial proliferation, "platelet" thrombi and simultaneous "glomerulitis." Gore suggested that the earliest prethrombotic lesion in thrombotic thrombocytopenic purpura is a swelling of the subendothelial hyaline material, followed by rupture of the endothelium, with deposition of platelets on the injured spot and formation of a bimorphic thrombus. Endothelial proliferation and organization of the thrombus would then take place, only to be followed by new depositions of platelets, bringing about thrombocytopenia. Two of his five patients had a leukemoid blood reaction. In most cases reported, a shift to the left, with immaturity, was noted in smears of peripheral blood, but leukemia was ruled out. The clinical picture is rather typical, although not specific for the condition.—K. O. Husebye, M.D., J. M. Stickney, M.D., and W. A. Bennett, M.D., "Platelet" Thrombosis in Leukemia, *Annals of Internal Medicine,* May, 1956.

ABO BLOOD GROUPS AND DISEASE

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• *The existence of an association between certain diseases and the ABO blood groups was investigated by studying the blood-type frequencies of 158 patients with pernicious anemia, 908 with gastric carcinoma, 1,839 with peptic ulcer, 866 with carcinoma of the breast, 395 with carcinoma of the lungs, 256 with carcinoma of the colon and rectum, 456 with leukemia, 327 with congenital anomalies, and 184 with ulcerative colitis, and comparing them with the blood-type frequencies observed in blood donors. The strongest association found concerned peptic ulcer; statistically significant associations also were found for gastric carcinoma and pernicious anemia. Patients with pernicious anemia were distributed between groups A and O in the ratio 1:0.78, while the control patients exhibited the ratio 1:1.10. So great a difference in a sample of this size would have been found as an accident of sampling less than 5 times in 100, and is therefore accepted as significant. The incidence of gastric carcinoma was also greatest in persons with blood type A; that of peptic ulcer was greatest in persons with blood type O. The data suggested, but did not suffice to prove, an association of blood group with pulmonary and mammary carcinoma. No evidence was found of association with carcinoma of the colon and rectum, leukemia, ulcerative colitis, or congenital anomalies.*

Although the first half of the 20th century has seen the rapid expansion of the science of genetics, there has not been comparable growth in that branch concerned with human inheritance. This is related to a long gestation period, small family size, and a scarcity of characteristics inherited in a sufficiently simple manner to make practical a study of the genetic mechanisms involved. Undoubtedly, the impossibility of bringing about experimental mating in humans has played a major part. The blood groups, however, provide the specialist in human genetics with an almost ideal tool for use in his studies. Being all-or-none characteristics, they are readily classified, and their method of inheritance is exactly known. A practical illustration of the latter is their use in paternity problems. That considerable thought has been given to the possibility of an association between the ABO blood groups and disease is indicated by the numerous reports since 1920. Most of the early studies were done elsewhere than the United States. The results of these investigations were conflicting and inconclusive. At the time of the comprehensive review by Lessa and Alarcao[1] in 1949, there still was no convincing evidence of such an association, although Levine, Katzin, and Burnham[2] in 1941 had demonstrated the role of rhesus blood types in erythroblastosis fetalis.

In 1951, Struthers[3] found that, in Scotland, there was an increased (higher than expected) frequency of blood type A among children dying of bronchopneumonia during the first two years of life. Widespread interest was kindled among geneticists, immunologists, general biologists, and clinicians by the report of Aird, Bentall, and Fraser Roberts[4] in 1953 indicating a highly significant increased frequency of blood type A and decreased (lower than expected) frequency of blood type O among 3,632 patients with gastric cancer in England and Scotland; similar findings were subsequently reported by Hollander[5] from Switzerland, Køster, Sindrup, and Seele[6] from Denmark, and our group[7] from the United States. In 1954, Aird and co-workers[8] reported data indicating an even more highly significant association with peptic ulcer characterized by an increase in O and decreases of the other blood-type frequencies in 3,011 patients. These findings were confirmed by Clarke and associates[9] in Great Britain, Køster, Sindrup, and Seele[6] in Denmark, and our group[10] in the United States. However, our results indicated no significant difference between duodenal and gastric ulcer, whereas the other investigators obtained dissimilar findings for the two; gastric ulcer did not show the highly significant increase in type O and decrease in type A noted for duodenal ulcer.[9] McConnell, Pyke, and Fraser Roberts[11] have found a significant increase in frequency of blood type A in male patients with diabetes mellitus in England, which they feel merits only a tentative conclusion of an association; there was no evidence of a similar association in women. Likewise, there does not appear to be an association to age of the patients, as was earlier suggested.

The failure of earlier studies to demonstrate the existence of the now-noted associations may be explained by the small size of the series, absence of disease specificity with regard to patient groups studied, unsatisfactory controls, and the failure to use proper methods of statistical analysis. However, since these considerations have been appreciated, in addition to the positive findings discussed above, the results of other, negative investigations have been reported. From England, in 1954, Aird and others[8] reported no association for carcinoma of the colon and rectum (2,599 cases), breast (1,017 cases), and bronchus (998 cases); McConnell, Clarke, and Downton,[12] in 1954, reported none for 777 cases of carcinoma of the lung. The initial evidence of an association of the ABO blood groups to toxemia of pregnancy has not been supported by later data collected by the same authors and Dickins and co-workers.[13] In 300

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Read before the Section on Preventive and Industrial Medicine and Public Health at the 105th Annual Meeting of the American Medical Association, Chicago, June 13, 1956.

cases of gynecologic cancer, Krokfors and Kinnunen[14] in Finland in 1954 were unable to find evidence of an association. Maxwell and Maxwell[15] in 1955 reported their findings indicating no association in 2,147 patients with essential hypertension in Scotland.

This report is concerned with the results of the investigations of the ABO blood-type frequencies in patients with several diseases at the State University of Iowa Hospitals. The authors of previous investigations done in the United States concluded there was no evidence for an association of the ABO blood groups and the diseases studied; these investigations are discussed in other communications.[16]

Clinical Material and Procedure

The case material was provided by patients seen at the University Hospitals, except for some of the cases of gastric carcinoma, peptic ulcer, and breast carcinoma, as will be indicated. To insure the high degree of homogeneity with regard to categories of disease vital to this study, only patients with ironclad diagnoses were included. Microscopic proof was required for the carcinomas, while unequivocal clinical findings were regarded as mandatory for other diseases. In addition to the diagnostic criteria, the only other factor acting to select cases was information concerning the patient's blood type. The case records of all patients with the various diagnoses made available by the record room files were reviewed and included if satisfying the two forementioned requirements. To eliminate possible errors resulting from collection by multiple investigators, we selected and recorded all the data. Innumerable statistical studies were made feasible by transferring the collected data to punch cards and then using machine methods for tabulation and sorting.

TABLE 1.—*Blood-Type Distribution in Groups Studied*

Blood Type	A University Hospitals Donors		B Des Moines Donors		C Controls*		D University Hospitals Patients†	
	No.	%	No.	%	No.	%	No.	%
O	2,149	45.8	743	45.8	2,892	45.8	1,124	45.8
A	1,953	41.7	672	41.4	2,625	41.6	1,000	40.8
B	423	9.0	147	9.1	570	9.0	246	10.0
AB	165	3.5	61	3.7	226	3.6	84	3.4
Total	4,690	100.0	1,623	100.0	6,313	100.0	2,454	100.0

* Combined data (col. A and B).
† Patients with peptic ulcers or neoplasms excluded.

TABLE 2.—*Blood Types in Controls and in Patients with Pernicious Anemia*

	Type O	Type A	Type B	Type AB	Total
Pernicious anemia	59	76	14	9	158
Controls	2,892	2,625	570	226	6,313
Totals	2,951	2,701	584	235	6,471

The procedure employed in analyzing the data was to compare the blood-type frequencies noted in groups of patients with those observed in a normal population sample. Healthy blood donors who were friends and relatives of the patients and who came from the same geographical area and had similar ethnological and anthropological origins were used. In table 1 are recorded the data collected by tabulating the blood types of consecutive blood donors at a Des Moines and the University Hospital blood bank. In column C are the combined data, which were used as controls for comparison with the blood-type frequencies noted in the patients. Note the close agreement of the blood-type frequencies of University Hospital patients receiving consecutive transfusions, excluding only those with diagnoses of peptic ulceration or malignancy, with those of the blood donors used as controls.

TABLE 3.—*Frequency of Types O and A in Patients with Pernicious Anemia and in Controls*

	O	A	Totals	Type A, %
Pernicious anemia	59	76	135	0.5630
Controls	2,892	2,625	5,517	0.4758
Totals	2,951	2,701	5,652	

The statistical significance of differences noted between the patients' and the controls' blood-type frequencies was tested by the chi-square method, which naturally weights the disease to match the size of the control group. An additional test in the form of the method of difference in percentages based upon the normal curve theory has been applied to the data at hand. In a consideration of the various methods of examining these data, comparison of the differences in the frequencies of the four blood types between patients and controls is the obvious and perhaps first one that should be applied. For example, let us examine all of the blood-type findings in the patient and control groups for pernicious anemia at the 5% level of significance (table 2). In this case chi square equals 6.772 with 3 degrees of freedom. Since the value of chi square at the 5% level of significance with 3 degrees of freedom is 7.815, we have a result that is not regarded as significant at the 5% level. However, we observe that $0.05<p<0.10$, and so it might be worthwhile to conduct an additional study involving more data or to examine these data in greater detail.

Since in the instance of each disease studied, more than 85% of the patients had blood type O or A, and since the major differences from the controls most often occurred in O and A, it was believed desirable to examine the data as to the statistical significance of the reciprocal changes in frequencies of the O and A blood types. This afforded an opportunity to compare the results with those of other investigators who for the most part have used this method of analysis.

TABLE 4.—*Blood Types in Patients with Gastric Carcinoma and Peptic Ulcer and in Controls*

	Blood Type O		Blood Type A		Blood Type B		Blood Type AB	
	No.	%	No.	%	No.	%	No.	%
Gastric carcinoma (908 cases)	383	42.2	416	45.8	84	9.2	25	2.8
Peptic ulcer (1,839 cases)	983	53.5	679	36.9	134	7.3	43	2.3
Controls (6,313 donors)	2,892	45.8	2,625	41.6	570	9.0	226	3.6

In particular, let us examine the frequencies with which types O and A occurred in the patients with pernicious anemia and compare them with the frequencies in the controls. The following 2 × 2 contingency table (table 3) states that among this total of 5,652 persons there were 59 who had pernicious anemia and whose blood was of type O. Calculations based on the subtotals show that, if there were no association between blood type and pernicious anemia, 65 patients would be expected to show this combination simply by chance, for 2,701 × 135/5,652 = 65 (approximately). But the figure actually found, namely, 76, exceeds the expected number by 11. The following calculation of chi square for a fourfold table (which has 1 degree of freedom) shows that so great a discrepancy between the actual and the expected would occur by chance less than 5 times in 100:

TABLE 5.—*Number of Patients with Carcinoma of the Breast by Blood Type and Hospital*

	Blood Type			
	O	A	B	AB
University Hospitals (571 cases)	244	253	56	18
Iowa Methodist Hospital (Des Moines) (138 cases)	57	63	9	9
Mercy Hospital (Iowa City) (157 cases)	69	67	16	5
Totals (866 cases)	370	383	81	32

$$X^2 = \frac{[(59)\,(2{,}625) - (76)\,(2{,}892)]^2\,(5{,}652)}{(2{,}951)\,(2{,}701)\,(135)\,(5{,}517)} = 4.012$$

From tables of chi square it can be seen that a value of 4.012 corresponds to a value of p between 0.02 and 0.05, and it can be asserted, therefore, that the frequency of blood type A was significantly higher among the patients with pernicious anemia than among the controls.

Further consideration based upon the difference in percentages based upon the normal curve theory:

$$t = \frac{0.5630 - 0.4758}{\sqrt{\dfrac{(0.5630)\,(0.4370)}{135} + \dfrac{(0.4758)\,(0.5242)}{5{,}517}}} = \frac{0.0872}{0.0477} = 1.83$$

yields a value that is slightly lower than that at the 5% level. However, any test that reveals a significant difference should not be overlooked. Consequently, this study suggests that the frequency of blood type A is significantly higher in patients with pernicious anemia than in the controls. In addition to the two methods illustrated, other comparisons taken two and three at a time (such as O and B or O and A and B) were made where indicated. Only the results of the first two comparisons will be reported.

TABLE 6.—*Blood Types of Patients with Carcinoma of the Breast*

Blood Type	Patients No.	Patients %	Difference in % from Controls	X^2	Level of Significance (Probability)
O	370	42.7	−3.1	2.861	$0.05 < p < 0.10$
A	383	44.2	+2.6	2.877	$p > 0.10$
B	81	9.4	+0.4		
AB	32	3.7	+0.1		
Total	866	100.0	0.0		

Results

The findings for patients with gastric carcinoma and peptic ulcer are summarized in table 4. When the blood-type frequencies noted in the patient and control groups were compared, levels of significance for the observed differences were noted at 2% for gastric carcinoma and 0.1% for peptic ulcer. The detailed data and discussion concerned therewith are included in other articles.[16] In table 5 are recorded the data, collected from three hospitals, relative to carcinoma of the breast. No significant differences were found between the blood-type frequencies of the patients from the different hospitals. For purposes of the further statistical analysis, these data were combined. The results of the O-A and the O-A-B-AB comparisons are recorded in table 6. Of interest is the chi-square value for the O-A comparisons indicating a level of significance at 10%, as compared with the O-A-B-AB comparison, where there was no evidence of significance.

Patients with carcinoma of the lung were studied as one sample and were not subdivided by cell type. As will be noted in table 7, the O-A comparison was significant at the 5% level. That is, the observed discrepancy between the expected and the actual would arise by accidents of sampling 5 times in 100. That it did so arise seems the more likely when one notices that, in the examination of the entire group, the differences among the four types could have arisen by chance 10 times in 100 and are therefore not to be considered significant. This may be due to the fact that the slightly increased AB and decreased B frequencies in the patients as compared with the controls balanced one another. The data with regard to patients with carcinoma of the colon and rectum appear in table 8. No evidence of statistical significance was discovered when comparisons of the O-A or the O-A-B-AB differences were made. When colonic (153 cases) and rectal (103 cases) carcinoma were examined separately, likewise no evidence of an association to blood type was found.

TABLE 7.—*Blood Types of Patients with Carcinoma of the Lungs*

Blood Type	Patients No.	Patients %	Difference in % from Controls	X^2	Level of Significance (Probability)
O	202	51.1	+5.3	4.643	$0.02 < p < 0.05$
A	144	36.5	−5.1	5.259	$p > 0.10$
B	33	8.4	−0.6		
AB	16	4.0	+0.4		
Total	395	100.0	0.0		

TABLE 8.—*Blood Types of Patients with Carcinoma of the Colon and Rectum*

Blood Type	Patients No.	Patients %	Difference in % from Controls	X^2	Level of Significance (Probability)
O	119	46.5	+0.7	0.120	$p > 0.10$
A	103	40.3	−1.3	0.283	$p > 0.10$
B	24	9.4	+0.4		
AB	10	3.8	+0.2		
Total	256	100.0	0.0		

Although most of the leukemias studied were either lymphatic or myeloid in type, small numbers of the less common ones were included. No evidence of an association to the ABO blood groups was found (table 9). The congenital anomalies studied have included those of the nervous, cardiovascular, respiratory, genitourinary, and gastrointestinal systems. Inspection of the combined data recorded in table 10 indicates that no statistically significant differences were found. Study of each separate group failed equally to show evidence of statistically significant differences. No evidence was found to suggest an association between the ABO blood groups and ulcerative colitis. These data are recorded in table 11. Although relatively few cases were available for study, evidence suggesting an association to the ABO blood groups, as already illustrated, was found in patients with pernicious anemia. These data are recorded in table 12. It will be noted that the evidence was strongest when the O and A comparison was made.

Comment

In the evaluation of the results of this or any similar study, reliable controls have been regarded as most important. This reliability is determined by whether or not the controls are truly representative of the population from which the patients came. For reasons stated in another article,[10] our controls would seem to compare favorably with those used by the other authors. The possible existence of unrecognized factors acting to select blood donors and thus altering the results of the comparisons with control patients has been considered. Whether blood donors are satisfactory controls and whether the concept of normal population controls for these investigations is valid are two questions not finally answered, which are the subject for continuing study.

TABLE 9.—*Blood Types of Patients with Leukemia*

Blood Type	Patients No.	Patients %	Difference in % from Controls	X^2	Level of Significance (Probability)
O	226	49.6	+3.8	1.732	$p > 0.10$
A	179	39.3	−2.3	3.575	$p > 0.10$
B	40	8.7	−0.3		
AB	11	2.4	−1.2		
Total	456	100.0	0.0		

TABLE 10.—*Blood Types in Patients with Congenital Anomalies*

Blood Type	Patients No.	Patients %	Difference in % from Controls	X^2	Level of Significance (Probability)
O	156	47.7	+1.9	0.046	$p > 0.10$
A	138	42.2	+0.6	2.147	$p > 0.10$
B	22	6.7	−2.3		
AB	11	3.4	−0.2		
Total	327	100.0	0.0		

As mentioned before, rigorous diagnostic criteria must be insisted on in categorizing patients for study. Patients who could not be regarded as having ironclad diagnoses were rejected. Pernicious anemia presented a particularly good example of this point. Although more than 600 cases were noted in the record-room files, only 158 of these patients were judged to have ironclad diagnoses, with achlorhydria, macrocytic hyperchromic anemia, megaloblastic bone marrow, and proper response to therapy. Absence of information relative to blood type eliminated a substantial number of patients.

The findings in gastric carcinoma agree with those reported by Aird, Bentall, and Fraser Roberts,[4] Hollander,[5] and Køster, Sindrup, and Seele.[6] Similarly, with the exception of the previously indicated difference in regard to gastric ulcer, our findings in peptic ulcer are in accord with those reported by Aird and co-workers,[8] Clarke and associates,[9] and Køster, Sindrup, and Seele.[6] Aird and co-workers [8] found no significance in the differences of the blood-type frequencies between controls and patients with carcinoma of the breast. Our finding indicating an increase in type A frequency of a level of significance at 10% for the O and A comparison is not to be interpreted as conclusive evidence of an association between mammary carcinoma and the ABO blood groups. It will be interesting to observe the results of future studies of this kind.

TABLE 11.—*Blood Types in Patients with Ulceratice Colitis*

Blood Type	Patients No.	Patients %	Difference in % from Controls	X^2	Level of Significance (Probability)
O	80	43.5	−2.3	0.552	$p > 0.10$
A	82	44.6	+3.0	0.773	$p > 0.10$
B	15	8.1	−0.9		
AB	7	3.8	+0.2		
Total	184	100.0	0.0		

A similar situation exists for lung carcinoma, for which Aird and associates [8] and McConnell, Clarke, and Downton [12] found no data of statistical significance. There is a need for study of more cases before proper interpretation at the 5% level of significance found for the O and A comparisons may be made. It is of interest that here, as in mammary carcinoma, comparison of the four blood-type frequencies rather than just O and A showed no statistically significant differences, the rather large differences in O and A frequencies being neutralized by absence of differences for types B and AB. In our series, 12.5% of 348 patients were Rh negative as compared with 15.7% of the controls; this difference is not statistically significant. There is an obvious need for collection of more data regarding this point.

TABLE 12.—*Blood Types of Patients with Pernicious Anemia*

Blood Type	Patients No.	Patients %	Difference in % from Controls	X^2	Level of Significance (Probability)
O	59	37.3	−8.5	4.012	$0.02 < p < 0.05$
A	76	48.1	+6.5	6.722	$0.05 < p < 0.10$
B	14	8.9	−0.1		
AB	9	5.7	+2.1		
Total	158	100.0	0.0		

The failure to find any evidence of significance for the differences observed in colonic and rectal carcinoma, leukemia, ulcerative colitis, and in patients with congenital anomalies, although not excluding the possibility of an association between these diseases and the ABO blood groups, makes it seem unlikely. In view of the similar findings of Aird and others [8] for carcinoma of the colon and rectum, the possibility of such an association in these disorders seems most unlikely. The findings reported by Tinney and Watkins,[13] in

1941, support the absence of any statistical significance for the data concerning leukemia. We are unaware of other similar data pertaining to ulcerative colitis or congenital anomalies.

Because of the heretofore recognized relationship between gastric carcinoma and pernicious anemia,[18] it is of a particular interest to note that evidence exists of an association to the ABO blood groups characterized by an increase in type A and decrease in type O frequency. These findings are in accordance with those of Aird [19] and differ from those of Køster, Sindrup, and Seele.[6] The implications of the association of pernicious anemia, gastric cancer, and the ABO blood groups, in view of the evidence of the role of heredity in gastric cancer,[20] are interesting and merit further investigation.

The level of statistical significance for the differences in the blood-type frequencies between the groups of controls and patients is a function of the size of that difference and the number of patients available for study. This latter factor has played a major role in our investigations, the size of our series of patients being limited by the number of patients (1) satisfying the diagnostic criteria and (2) for whom blood-type information was available. In the instance of each disease studied, with the possible exception of duodenal ulcer, it would have been desirable to have had more cases. However, from a practical point of view it is apparent that the investigator in the instance of each disease can have only a finite number of cases. Although the results based upon a relatively small number of cases are often inconclusive, two purposes may be served in reporting them. The findings may indicate the need for collection of more data or, when they are added to series already collected, may result in convincing evidence of a previously suspected association. Conversely, a previously suspected association may be made less acceptable. A real danger exists, however, of drawing unwarranted conclusions from series of insufficient size, serving thereby to confuse and discredit these researches.

The findings concerning gastric cancer, peptic ulcer, and pernicious anemia support the attractive hypothesis of a relationship between the ABO blood groups and the pathological physiology of the stomach and duodenum in these patients. The evidence of a relationship to the secretion of free hydrochloric acid [10] fits nicely with this concept. It remains to be proved that ulcerogenic and carcinogenic or, conversely, protective attributes are exercised by the mucopolysaccharide blood group substances.

The evidence of associations for diseases not related to the gastrointestinal tract suggests that the association of blood group and disease may be related to broad anatomic, biochemical, and physiological considerations, thus relating disease and heredity. A possible role in natural selection is suggested for the ABO blood groups by these findings. Whether these and other speculations have basis in fact must await the collection of more data, with careful adherence to the criteria that have been established, and the results of basic investigations of the underlying mechanisms. Although the possibility that the findings merely indicate a chance association between the ABO blood groups and disease rather than a causal relationship becomes less likely with the report of each group of data confirming the association, the former possibility has not as yet been excluded. Likewise, an anthropological explanation based on the possibility that there are population strains with high or low incidences of certain diseases becomes progressively less tenable with the accumulation of similar data from different population groups throughout the world.

Summary

Conclusive evidence of an association between the ABO blood groups and disease has been found. Gastric carcinoma occurs more frequently in persons with blood type A than in those with the other blood types, peptic ulcer more frequently in those with blood type O, and pernicious anemia more frequently in those with blood type A. No evidence of such an association was found in patients with carcinoma of the colon and rectum, leukemia, ulcerative colitis, or those with congenital anomalies. In cancer of the lung and breast, more data will need to be collected before the equivocal findings may be properly interpreted; in view of the failure of other investigators to find evidence for an association, much more convincing data must be collected before the possibility of associations for these diseases may be claimed.

Addendum

Since this article was submitted for publication, in addition to the associations for gastric carcinoma and pernicious anemia we have found evidence of associations between rheumatic heart disease, hip fracture, and the ABO blood groups. Evidence has also been found of similar associations in a Negro population group.

This study was supported in part by a grant from the American Cancer Society.

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PEPTIC ULCERATION AND ABO BLOOD GROUPS

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• *The incidence of the four blood types O, A, B, and AB was studied in 1,301 patients with duodenal ulcer, 469 with gastric ulcer, and 69 patients with both gastric and duodenal ulcers. The three distributions so obtained were compared with the distribution found in a reference of 8,767 people without ulcers. Type O was more frequent among the ulcer patients than in the reference group, and calculations of probability showed that the association between type O and peptic ulcer was statistically significant. It was shown not to be secondary to any influences of sex, age, rhesus blood type, or occupation. Among a group of 529 patients who had histamine tests, however, the frequency of type O was significantly greater among those who reacted with an increase of free hydrochloric acid than among those in whom no increase of acid occurred.*

In 1921, 21 years after Landsteiner's [1] classic blood-group work, Buchanan and Higley [2] reported a study of the possible relationship of the ABO blood groups to various diseases, including peptic ulceration. These authors concluded that there was no relationship to any disease for which sufficient data were available to justify a conclusion. The data reported by Ugelli [3] in 1936 and Lessa and Alarcao [4] in 1949 show an increased (higher than expected) frequency of blood type O in patients with peptic ulcer. The failure to recognize the significance of these data may be attributed to the difficulty in obtaining suitable population control groups, a preoccupation with the study of multiple diseases, the small size of the series, and a failure to apply suitable methods of statistical analysis. In 1954, Aird and co-workers [5] demonstrated convincingly that a highly significant relationship exists between peptic ulceration and the ABO blood groups in Great Britain. Their data indicate that persons with blood type O are about 35% more likely to develop peptic ulceration than are those with the other types. Similar findings have since been reported by Clarke and associates [6] from Liverpool and Køster, Sindrup, and Seele [7] from Denmark.

The initial effect of these observations has been to give interested clinical and basic investigators alike a sense of fulfillment of the expectation, based on genetic considerations, that the relationships between diseases and blood groups that should exist, do in fact. Ford [8] hinted at this in suggesting the possible relationship of blood groups to natural selection. It is possible that a door has opened through which a way may be seen to further research leading to the solution of heretofore unfathomable problems related to the broad considerations of disease and heredity. As yet, satisfactory explanations for the observed phenomena have not been provided. The immediate need is for the collection of similar data from other population groups throughout the world. The present report concerns such investigations carried out in the United States; the authors of two previous reports from this country concluded that there was no association between the ABO blood groups and peptic ulceration.[9]

Materials and Methods

The bulk of the clinical material for this study was provided by patients admitted to the University Hospitals from 1940 to 1956. Five other Iowa hospitals provided the remainder. Data obtained from the Iowa City and Des Moines blood banks have been used to determine the frequency of blood types in the population from which the patients came. Since the percentage of Negroes among the blood donors did not differ significantly from the 2.1% noted among the otherwise Caucasian patient groups, race did not contribute to the observed differences in blood-type frequency. In table 1, columns A and B, are recorded the number of individuals of each blood type and the percentage of the total group this number represents (subsequent-

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ly referred to as blood-type percentage). Since there were no significant differences noted between the Iowa City and Des Moines donors in regard to the ABO group frequencies, they have been pooled and are henceforth referred to as controls (column C). A further indication of the reliability of these donor groups as representative population samples is provided by a comparison of the blood-type frequencies noted with those of a random sample of patients at University Hospitals, with only those with peptic ulcer and neoplastic disease excluded (table 1, column D). Statistical analysis of these data has been completed by methods to be described.

TABLE 1.—*Blood-Type Distribution in Groups Studied*

Blood Type	A University Hospitals Donors		B Des Moines Donors		C Controls*		D University Hospitals Patients†	
	No.	%	No.	%	No.	%	No.	%
O	2,149	45.8	743	45.8	2,892	45.8	1,124	45.8
A	1,953	41.7	672	41.4	2,625	41.6	1,000	40.8
B	423	9.0	147	9.1	570	9.0	246	10.0
AB	165	3.5	61	3.7	226	3.6	84	3.4
Total	4,690	100.0	1,623	100.0	6,313	100.0	2,454	100.0

* Combined data (Col. A and B).

† Patients with peptic ulcers or neoplasms excluded.

To ensure reliability of the data, it was essential to establish sound diagnostic criteria, which were then painstakingly applied in the selections of the cases. Either an anatomic or an ironclad clinical diagnosis of peptic ulcer was required. *In the patients with* anatomic diagnoses, comprising more than 80% of the clinical material, the diag*nosis was established* at the time of operation by gross and/or microscopic findings. The surgeon's operative note and pathologist's reports were the source of this information. Differentiation of duodenal from gastric ulcer was similarly determined; a third group of patients having both duodenal and gastric ulcers was included. Patients having lesions located at the pylorus, in whom it was impossible to determine whether the ulcer was duodenal or gastric, were excluded. By ironclad clinical diagnosis is meant a convincing history and positive evidence of ulcer on radiological and/or gastroscopic examination.

TABLE 2.—*Type of Ulcer, Blood Type, and Hospital of Patients Studied.*

Ulcer	Blood Type	Hospitals: Iowa City: University	Hospitals: Iowa City: Veterans*	Hospitals: Iowa City: Mercy	Hospitals: Des Moines: Methodist	Hospitals: Des Moines: Broadlawns	Total
Duodenal	O	382	155	66	52	43	698
	A	250	110	45	42	25	472
	B	53	26	10	9	4	102
	AB	16	7	1	3	2	29
	Total	701	298	122	106	74	1,301
Gastric	O	175	30	17	15	11	248
	A	117	20	19	11	13	183
	B	18	2	3	2	1	26
	AB	10		1	1		12
	Total	320	52	40	32	25	469
Duodenal and gastric	O	24	4	6	1	2	37
	A	15	3	5	1		24
	B	4		1	1		6
	AB	1			1		2
	Total	44	7	12	4	2	69
Totals	O	581	189	89	68	56	983
	A	382	133	69	57	38	679
	B	75	28	14	12	5	134
	AB	27	7	2	5	2	43
	Total	1,065	357	174	142	101	1,839

* Data from Iowa City and Des Moines veterans hospitals combined.

To eliminate possible errors resulting from collection by multiple investigators, a team composed of three of us (E. B. W., D. C. C., and J. A. B.) selected and recorded all the data. On a separate card for each patient was recorded the desired information culled from the patient's case record. This included the following: identifying information, age, year seen, sex, race, occupation, primary and secondary diagnoses, method of diagnosis and treatment, gastric acidity, histamine-test response, Rh blood type, and, most important, the ABO blood group. Innumerable correlation studies were made feasible by the transference of the collected data to IBM punch cards and the use of machine tabulation and sorting methods.

TABLE 3.—*O-A and O-A-B-AB Comparisons for All Patients with Ulcer*

Ulcer	Blood Type	Patients: No.	Patients: %	Difference in % from Controls	X^2	Level of Significance (Probability)
Duodenal	O	698	53.7	+7.9	20.340	$p<0.001$
	A	472	36.3	−5.3	29.573	$p<0.001$
	B	102	7.8	−1.2		
	AB	29	2.2	−1.4		
	Total	1,301	100.0	0.0		
Gastric	O	248	52.9	+7.1	4.206	$0.02<p<0.05$
	A	183	39.0	−2.6	12.905	$0.001<p<0.01$
	B	26	5.5	−3.5		
	AB	12	2.6	−1.0		
	Total	469	100.0	0.0		
Duodenal and gastric	O	37	53.6	+7.8	1.641	$p>0.10$
	A	24	34.8	−6.8	1.662	$p>0.10$
	B	6	8.7	−0.3		
	AB	2	2.9	−0.7		
	Total	69	100.0	0.0		
All ulcers	O	983	53.5	+7.7	23.258	$p<0.001$
	A	679	36.9	−4.7	37.049	$p<0.001$
	B	134	7.3	−1.7		
	AB	43	2.3	−1.3		
	Total	1,839	100.0	0.0		

The only factors affecting case selection were our diagnostic criteria and the availability of blood-typing information. Through the record room files of the respective hospitals, the records of all patients with a diagnosis of peptic ulcer were scrutinized. Only one in six patients with a clinical diagnosis met our requirements and could be included in the study. In examination of the data, comparison has been made of the frequency of each blood type observed in the disease and control samples. The statistical significance of observed differences has been tested by the chi-square method, which naturally weights the disease to match the size of the control group. Aird and co-workers[5] have amply discussed the importance of this latter calculation in making most efficient use of the data at hand. The validity of the analyses has been further tested by application of the method of differences in percentages based upon the normal curve theory.

Results

In table 2 are recorded the numbers of patients, tabulated by hospital and lesion, with each blood type. Comparison of the data collected from the individual hospitals, with the exception of the University Hospitals, would appear to be meaningless because of the small numbers of patients. No significant degree of heterogeneity was shown to exist between the hospital groups. Therefore, in the further examination of the data, those data from the six hospitals have been combined and are considered as one sample.

TABLE 4.—*Blood Types O and A with Reference to All Patients with Ulcers and to Controls*

	Blood Type			
	O	A	Totals	Type O, %
All ulcers	983	679	1,662	59.15
Controls	2,892	2,625	5,517	52.42
Totals	3,875	3,304	7,179	

The blood-type frequencies observed in patients with duodenal, gastric, and both ulcers were compared with those of the controls. For those who desire to do so, gene frequencies may be calculated by Fisher's method as described by Dodson and Ikin,[10] which is merely another way of presenting the data *showing the same relationships*. In table 3 are recorded the numbers of patients with each blood type by lesion, blood-type percentages, the increase or decrease of blood-type percentage of the disease as compared with the control group, chi-square values for the O-A and the O-A-B-AB comparisons, and the levels of significance indicated. A reciprocal difference is observed in the relative portions of the O and A types. When the data were analyzed by O-A, O-A-B, O-A-B-AB comparisons, etc., it became apparent that the simplest, most practical method of analysis was to study the significance of the reciprocal changes noted in the O and A blood-type frequencies. This is because the greatest discrepancies occur in blood type O and also because about 85% of the patients have either O or A blood type. Since this type of analysis has been used by previous workers, it also affords an opportunity to compare our results with those of similar studies being reported from different areas of the world. Since the other comparisons added little interest to the present discussion, only two results are recorded in the table, namely (1) the relative frequencies of types O and A and (2) the relative frequencies of types O, A, B, and AB.

For an example, suppose we examine the relationship of the blood types O and A with respect to ulcers of all types (table 4).

The calculation (1,662)(3,875)/7,179=897 shows that, if there were no relationship between blood group and ulcers, in a sample of this size one would expect to find ulcers in 897 patients of type O, purely as a matter of chance. In reality there were 983. The difference between the actual and the expected figures is therefore 86. The probability that so great a difference might occur simply as an accident of sampling is found by the following computation of chi square:

$$X^2 = \frac{[(983)\ (2,625) - (679)\ (2,892)]^2\ (7,179)}{(1,662)\ (5,517)\ (3,875)\ (3,304)} = 23.26$$

A 2 × 2 contingency table has one degree of freedom. From tables of chi square one obtains, for 1 degree of freedom and a chi-square value of 23.26, a value of p less than 0.0005. This means that it is extremely unlikely that the above difference arose purely by chance; the difference is highly significant. We therefore assert that the incidence of ulcers of all kinds was significantly higher in patients with type O than type A blood, or that the incidence of type O among patients with ulcers of all kinds was higher than among the controls. This result is confirmed by the use of method of differences in percentages based upon the normal curve theory:

$$t = \frac{0.5915 \quad - \quad 0.5242}{\sqrt{\frac{(0.5915)\ (0.4085)}{1,662} - \frac{(0.5242)\ (0.4758)}{5,517}}} = \frac{0.0673}{0.0138} = 4.88$$

which again is highly significant since the value of t is greater than 3.

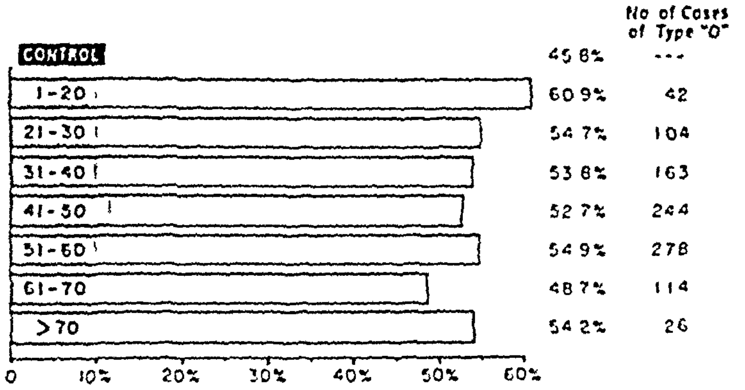
Notice that differences of the greatest magnitude, similar for each of the patient groups, occurred with regard to blood type O. Note the negative differences of lesser magnitude for the other three blood types in each group of patients. Disparity in the size of samples of patients is chiefly responsible for the differing levels of significance (probability) for the three groups, and it is possible that, if a comparable number of patients with gastric or both gastric and duodenal ulcers had been available, significant differences comparable to that for duodenal ulcer might have been observed. In the succeeding treatment of the data concerned with the specific characteristics of the groups of patients, the patients with duodenal, gastric, and both

TABLE 5.—*O and A Blood Types with Regard to Various Factors*

Row	Factors	Patients No.	Blood Type	Patients No.	Patients %	Difference in % from Controls	X^2	Level of Significance (Probability)
1	Rhesus +	1,228	O	656	53.3	+7.5	0.883	p>0.10
			A	444	36.2	−5.4		
	Rhesus −	245	O	126	51.5	+5.7		
			A	98	40.0	−1.6		
2	Men	1,194	O	637	53.4	+7.6	0.849	p>0.10
			A	449	37.6	−4.0		
	Women	276	O	157	56.8	+10.7		
			A	97	34.9	−6.7		
3	Anatomic diagnosis	1,540	O	834	54.1	+8.3	2.391	p>0.10
			A	553	35.9	−5.7		
	Clinical diagnosis	299	O	151	50.5	+4.7		
			A	124	41.5	−0.1		
4	Surgical treatment	1,372	O	740	53.9	+8.1	0.161	p>0.10
			A	504	36.7	−4.9		
	No surgical treatment	429	O	224	52.2	+6.4		
			A	160	37.3	−4.3		
5	Free hydrochloric acid high	581	O	332	57.1	+11.3	1.254	p>0.10
			A	209	36.0	−5.6		
	Free hydrochloric acid low	223	O	116	52.0	+6.2		
			A	88	39.5	−2.2		
6	Hydrochloric acid high with operation	521	O	297	57.0	+11.2	1.696	p>0.10
			A	187	35.9	−5.7		
	Hydrochloric acid low with operation	191	O	101	52.9	+7.1		
			A	76	39.8	−1.8		
	Hydrochloric acid high without operation	60	O	35	58.3	+12.5		
			A	22	36.7	−4.9		
	Hydrochloric acid low without operation	32	O	14	43.8	−2.0		
			A	13	40.6	−1.0		
7	Free hydrochloric acid increased	414	O	230	55.6	+9.8	4.443	0.02<p<0.05
			A	149	36.0	−5.6		
	After histamine not increased	115	O	49	42.6	−3.2		
			A	51	44.3	+2.8		

ulcers have been combined and are considered as one sample. This was desirable not only because it simplifies the presentation but also because the possibility that a statistically significant relationship would be missed as a result of insufficient numbers of patients in a sample was thus reduced. When indicated, independent analyses for each group were done.

In view of findings that indicated an association between peptic ulcer and the ABO blood groups, it became important to explore the possibility that certain characteristics of these patients might have a relationship to the demonstrated association. Such a relationship would offer additional support for the main association and might provide a promising approach leading ultimately to an understanding of the causes responsible. In table 5 are recorded the data relative to Rh blood types, sex, methods of diagnosis, treatment, and gastric acidity. The numbers of patients for whom such information was available are indicated; in none of the categories studied was such information obtained for all 1,839 patients with ulcers. Here, likewise, the reciprocal changes in O and A frequencies were employed in analysis of the data.



Percentage of patients with peptic ulcer with blood type O, by decade of age. The frequency of type O among patients of all ages was 53.5%, while it was 45.8% for the controls.

Changes in B and AB frequencies were as expected; the analyses of the B and AB changes added nothing to our present considerations and are not recorded.

Of the 1,473 patients in whom the Rh blood type was determined, 1,228, or 83.4%, were Rh positive; when this was compared with the 84.3% noted in the controls, no significant difference was found. When the same analysis was performed for each blood type, i. e., comparison of positive and negative in patients and controls with blood type O, etc., no significant difference was found. These data were examined in another way in row 1, where the ABO blood-type frequencies noted within the positive and negative groups were compared; again, no significant difference was demonstrated. It may be concluded that Rh type appears to have no relationship to the ABO blood group–peptic ulcer association.

With those from the two Veterans Administration hospitals excluded, there remained 1,472 patients, of which number 1,194, or 81.1%, were men. Row 2 shows that there was *no significant* relationship between sex of the patient and the ABO blood group–peptic ulcer association. As has been stated, in addition to the bulk of patients with diagnoses established at the time of surgery, those with ironclad clinical diagnoses were included. Although comparison of these two groups, in row 3, indicates a higher frequency of blood type O in those patients with surgical diagnoses, no significant difference was demonstrated. Likewise, none was found when patients treated with and without surgery were compared (row 4).

Information concerning gastric analysis, specifically that concerned with free hydrochloric acid, was obtained for 804 patients. After scrutinizing the data regarding degrees of free acid, we decided that the most meaningful method of analysis was to compare those patients with decreased or negligible amounts of free acid and those with normal or increased amounts. Row 5 shows that the apparent differences in blood-type frequencies do not indicate a significant difference. When these two groups of patients are subdivided into those treated with and without surgery, in row 6, it is of interest to observe the O and A frequencies similar to those of the controls in the small group of patients with low acid and no surgery; no statistical significance was demonstrated in the analysis of the four subgroups; 3 degrees rather than 1 degree of freedom were present. When the 529 patients who had histamine tests performed are studied (row 7), there is seen to be a significant difference, indicating that those having an increase in free acid, as compared with those having no increase in free acid, have a stronger association between the ABO blood groups and peptic ulceration. When the blood-type percentages of the patients with ulcers were examined by decade of age, nothing was found to suggest a relationship of age to the ABO blood groups–peptic ulcer association. This is illustrated in the figure by the absence of significant differences in blood type O frequency when the various decades are compared; similarly, no significance was noted for blood types A, B, and AB. Occupation and social and economic status were studied and appeared equally devoid of significance.

Comment

Of the foremost importance in the interpretation of the findings of this study is the degree of homogeneity or heterogeneity of the controls and patients. In this respect, a relatively stable agricultural population would seem to have advantage in providing source material, as compared with the constantly shifting population found in metropolitan and urban areas, which must necessarily result in relatively more heterogenous groups of controls and patients. Our controls and patients were relatives or friends, with similar genetic, ethnic, and anthropological origins, coming from the same geographical region. A relatively insignificant number of first-generation and second-generation immigrants, from other countries or from elsewhere in the United States, are included. Evidence of the high degree of homogeneity is provided by similar blood-type frequencies observed in the two groups of blood donors and the similar findings noted in an unselected group of patients, with only those with peptic ulcer and neoplastic disease excluded. The use of patients from several hospitals with similar facilities and standards of clinical practice and drawing their patients from the same population group would seem to reduce the chance that the results would be distorted by screening factors related to any one hospital.

The most important single point that emerges from this study is the close agreement of the findings with those previously reported. The level of statistical significance of the association between peptic ulceration and the ABO blood groups is of the same high degree reported by Aird and associates[5] and Clarke and associates[6] in Great Britain and Køster, Sindrup, and Seele[7] in Denmark. Since the Iowa population is derived chiefly from northern European stock, rather minor anthropological differences probably exist between the samples studied. However, in table 6 it will be noted that real differences in blood-type frequencies in controls do exist; for example, of British and Danish controls, 47.1 to 49% and 40.6%, respectively, had blood type O. With each new population group studied, the attractive hypothesis that the findings have an anthropological basis related to population strains with high and low incidence of certain diseases becomes less tenable. However, it may be abandoned only if the results of similar studies conducted in anthropologically dissimilar populations confirm the reported findings. Such studies would also provide strong evidence that there is causal relationship between the ABO blood groups and peptic ulceration rather than just an association.

Our failure to find significant differences between patients with duodenal and gastric ulcers is in sharp disagreement with the findings of Clarke and coworkers[6] and to a lesser extent with those of others. Our findings of a relatively higher frequency of type O than was found by the other workers in gastric ulcer, coupled with a relatively decreased one in duodenal ulcer, are of interest. In table 6 are recorded the data reported by the various investigators (macroscopic diagnosis of duodenal and gastric ulcer) showing the increase or decrease in blood-type percentages of patient groups as compared with the control group. In view of the close agreement noted in duodenal ulcer, it is difficult to find a plausible explanation for the differences observed for gastric ulcer. The accumulation of additional data from these and other sources should ultimately provide the answer to this question.

Of the many avenues that suggest themselves for study, one of the most promising would seem to be the study of the possible relationship of the secretion of blood-type substances. Such data should permit testing of the hypothesis of the possible protective or ulcerogenic effects exercised by these substances upon the mucous membranes of the stomach and duodenum. The possibility exists that as yet undiscovered red blood cell or other associated and similar antigens linked to known type-specific substances may act locally or systemically, being responsible for the findings. Our results suggest that ulcer patients with higher levels of free hydrochloric acid have higher frequencies of blood type O than those with lower acid levels; this could be related to local tissue factors or to more fundamental individual differences. The findings of Struthers[11] and McConnell,[12] as well as our own findings,[13] suggest the existence of similar relationships between the ABO blood groups and disorders other than those of the gastrointestinal tract. This may be a clue suggesting that we are dealing with basic anatomic, biochemical, and physiological differences related to the genetic make up of the individual and, thus, linked to the ABO blood group.

The findings relative to the various clinical characteristics studied are difficult to interpret. Although statistical significance has been shown to exist only for the histamine studies, the total findings related to gastric acidity suggest a relationship here and indicate a need for the collection of more data. In view of a chi-square value approaching a level of significance when comparison of those patients with clinical and surgical diagnoses is made, it is of interest to speculate regarding the possible meaning of these findings. The most interesting and challenging suggestion is that this may be evidence that the ulcer diathesis is more severe in patients with type O than any other type, leading more often to surgical therapy. More probable is the possibility that not all clinical diagnoses were ironclad and thus an unknown number of patients without ulcer were included, lowering the frequency of blood type O in the group with clinical diagnoses. Collection of more data should provide more satisfying answers regarding the possible relationship of these clinical characteristics to the ABO blood groups–peptic ulcer association.

TABLE 6.—*Data Regarding Macroscopically Diagnosed Duodenal and Gastric Ulcers Reported by Several Investigators*

Investigator	Blood Type	Duodenal Ulcer No.	Duodenal Ulcer %	Controls, %	Difference in % from Controls	Gastric Ulcer No	Gastric Ulcer %	Controls, %	Difference in % from Controls
	O	1,048	56.6	47.1	+9.5	538	53.0	46.9	+6.1
Aird	A	616	33.3	40.9	—7.6	376	37.0	41.1	—4.1
and	B	141	7.6	9.0	—1.4	77	7.6	8.9	—1.3
others[5]	AB	46	2.5	3.0	—0.5	24	2.4	3.1	—0.7
Total		1,851	100.0			1,015	100.0		
	O	505	58.7	48.9	+9.8	185	49.1	49.0	+0.1
Clarke	A	263	30.6	39.1	—8.5	151	40.1	39.1	+1.0
and	B	62	7.2	9.5	—2.3	31	8.2	9.4	—1.2
others[6]	AB	30	3.5	2.5	+1.0	10	2.6	2.5	+0.1
Total		860	100.0			377	100.0		
	O	342	50.3	40.6	+9.7	176	46.3	40.6	+5.7
Køster	A	261	38.4	44.0	—5.6	139	41.2	44.0	—2.8
and	B	60	8.8	10.9	—2.1	28	8.3	10.9	—2.6
others[7]	AB	17	2.5	4.5	—2.0	14	4.2	4.5	—0.3
Total		680	100.0			337	100.0		
	O	569	54.4	45.8	+8.6	231	53.5	45.8	+7.7
Present	A	370	35.3	41.6	—6.3	164	37.9	41.6	—3.7
study	B	85	8.1	9.0	—0.9	25	5.8	9.0	—3.2
	AB	23	2.2	3.6	—1.4	12	2.8	3.6	—0.8
Total		1,047*	100.0			432*	100.0		

* The discrepancy with table 3 results from the exclusion of patients with ulcers in whom the diagnosis was established by nonsurgical methods

At this time, the explanation for and meaning of the observed association between peptic ulceration and the ABO blood groups remains in the realm of speculation. Although the current evidence does not permit any conclusions to be drawn regarding the possible relationship of these findings to the etiology and pathogenesis of peptic ulceration, a promising new territory has been opened up, exploration of which may ultimately provide some of the long-sought answers to these and other equally pressing questions. As noted in our preliminary report,[14] the findings do suggest that the ABO blood groups may well participate in the process of natural selection.

Summary

In a comparison of the frequencies of the ABO blood types of 1,839 patients with duodenal and/or gastric ulceration with those observed in a representative sample of the population from which the patients came, a highly significant association was noted to exist between the ABO blood groups and peptic ulceration, characterized by an increase in O and reciprocal decreases in the three other blood-type frequencies; the findings are similar for duodenal and gastric ulceration. The level of free hydrochloric acid and whether the diagnosis was anatomic or clinical may possibly have a definite relationship to the association observed, while sex, age, rhesus blood type, and occupation appear to have none.

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EXPERIENCE WITH ARTERIAL HOMOGRAFT BANK

REPORT OF ONE HUNDRED CONSECUTIVE ARTERIAL HOMOGRAFTS

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• *An arterial homograft bank was established to supply freeze-dried segments of human arteries for use in surgery. Analysis of the results from the first 100 preparations used shows that 36 were used in repairing aneurysms of the abdominal aorta and 24 in relieving arteriosclerotic obstruction in peripheral arteries, with results considered good in 24 and 20 cases respectively. Uniformly good results were obtained in 13 cases of obstruction of the terminal portion of the aorta and 11 cases of coarctation. Mortality was high in ruptured, but low in unruptured, aneurysms of the abdominal aorta. The preparation of materials for the arterial homograft bank can be undertaken by large community hospitals without additional highly trained personnel.*

Many of the technical surgical procedures requiring the use of arterial homografts and the maintenance of arterial homograft banks can easily be provided by large community hospitals without additional highly trained personnel. To encourage others to establish similar banks, the following experiences are presented. An artery bank was first established at the Hospital of the University of Pennsylvania in 1953. A description of methods of preservation that have been used and an analysis of the results of the first 100 consecutive cases in which grafts from this bank were used is presented. This bank has supplied the needs of the Hospital of the University of Pennsylvania and on request has now supplied grafts to 24 other hospitals in the surrounding area. These institutions are in turn asked to help in procuring other grafts.

Methods of Preservation of Grafts

When the bank was established, freeze-drying was selected as the method of preservation and a freeze-drying unit was built.[1] It was of simple construction (fig. 1), and the total cost of the equipment was less than $500. It has required essentially no maintenance. Originally the grafts were all obtained under sterile precautions from fresh cadavers free of infection or malignant disease and were then placed in lactated Ringer's solution, to which antibiotics were added. The grafts were then refrigerated until the freeze-drying process was started. The freeze-drying was accomplished by quick freezing in a mixture of acetone and dry ice, and then the grafts were dried for 36 hours at low pressure (50 to 150 μ Hg). The grafts were then stored in test tubes sealed with rubber stoppers and capped with sealing wax after evacuation of the tube to a pressure of approximately 150 μ.

In the last year this method has been modified in several ways. The grafts are no longer taken under sterile conditions, and any human arteries not showing gross abnormality are considered suitable. Before freeze-drying, the grafts are sterilized with a 1% solution of beta-propiolactone, according to the method

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developed by Szilagyi and co-workers.[2] Grafts are now kept in sealed glass tubes ridged in order that they may be snapped open easily when needed (fig. 2). These grafts are then reconstituted in 0.9% saline solution, and their branches are tied off with suture ligatures after reconstitution. Prior to the use of sterilization of the grafts, it had become exceedingly difficult to obtain an adequate supply of grafts that fulfilled our criteria. Since the change in method of procurement and sterilization, some of these difficulties have been encountered with less frequency, and, as more interest has developed in the use of arterial homografts, it is becoming easier to obtain material.

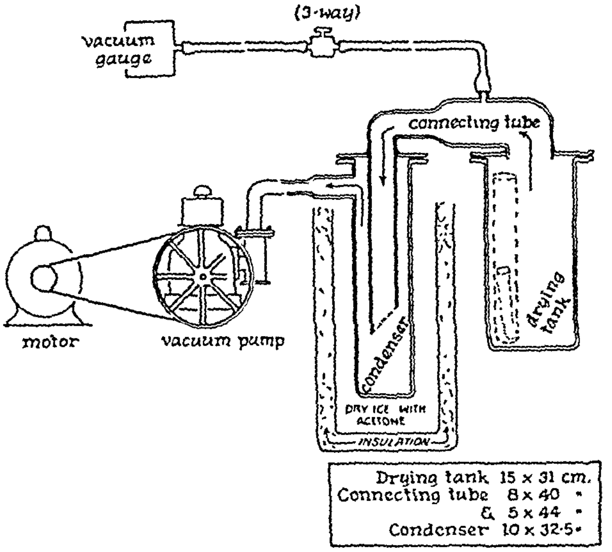

Fig. 1.—Diagram of freeze-drying apparatus.

The sealing of the grafts in glass ampuls has several advantages over the older method: the loss of vacuum that occurred in 10 to 20% of the test tubes when sealed with wax and rubber stoppers is prevented; the danger of contamination is reduced at the time the ampul is opened; and it is possible to sterilize the ampul itself by chemical means so that it can be handled freely by the surgeon. This procedure does, however, require the services of an experienced glass blower, and, if such is not available, rubber stoppers and sealing wax can still be used to obtain a satisfactory seal.

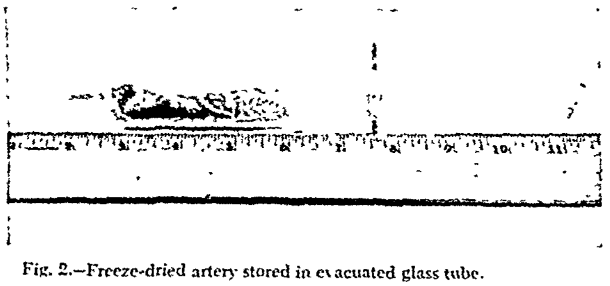

Fig. 2.—Freeze-dried artery stored in evacuated glass tube.

Results with First 100 Grafts

In the table we have tabulated the results obtained from the use of the first 100 consecutive grafts from the bank. It has been possible to obtain follow-up data from every patient in whom they were used. The operative procedures were carried out by 17 different surgeons in 10 different hospitals, but 79 of the 100 grafts were used in the Hospital of the University of Pennsylvania. This table shows a representative cross section of the use of arterial homografts in vascular surgery today. In the analysis of these data we have listed results as good when there was definite improvement after the operation. For example, in patients with obstruction of the terminal portion of the aorta (Leriche's syndrome), if the circulation to both feet was improved after the operation the results have been called good even though pulses may not have been restored to the feet. The results have been listed as fair if the patient has been harmed in some manner even though the over-all result has been an improvement, i. e., after successful removal of an abdominal aneurysm, one patient had a small embolus that blocked one anterior tibial artery and he lost portions of three toes. When the operative procedure resulted in further loss of circulation but not in death, the results have been listed as poor. The patients who died within 30 days after operation have been listed under the column "Died."

Results Obtained from Use of 100 Arterial Homografts at Hospital of the University of Pennsylvania

Disease for Which Graft Used	Total	Good	Fair	Poor	Died
Aorta					
Abdominal aneurysms	36	24	1		11
Thoracic aneurysms	4	2			1
Coarctation	11	11			
Obstruction of the terminal portion of the aorta (Leriche's syndrome)	13	13			
Saddle embolus	1				1
Peripheral arteries					
Arteriosclerotic obstruction	24	20	1	3	
Aneurysm	4	3		1	
Tetralogy of Fallot (Blalock operation)	2	2			
Trauma	3	2		1	
Tumor	1	1			
Thrombosis, superior vena cava	1			1	
	100	79	2	6	13

Examination of the results in abdominal aneurysms shows an operative death rate of 30%. Seven of the 11 deaths, however, occurred in nine patients with ruptured abdominal aneurysms—a group in whom the mortality is inevitably high. In the last 23 consecutive patients having unruptured abdominal aneurysms, there has only been one operative death—a mortality rate of less than 5%. The four patients who died after removal of unruptured aneurysms died of the following causes: (1) pulmonary embolus, (2) uremia, (3) myocardial failure after resuscitation of cardiac arrest while under anesthesia, and (4) rupture of the graft on the 28th postoperative day. This graft failure was the only one encountered in this series of 100 cases and occurred as a longitudinal split at the proximal suture line. There is some question about the reconstitution of this graft, in that it is believed to have been handled before it was completely reconstituted.

Among the patients having coarctation of sufficient length to preclude end-to-end anastomosis, the results of grafting have been excellent. Gross,[3] in a larger series, has also reported good results. We likewise have had satisfactory results in the use of these grafts in patients having the tetralogy of Fallot. Homografts from the bifurcation of the aorta were inserted in 13 patients with obstruction of the terminal portion of the aorta, and all showed some improvement postoperatively.

In the table we have classified the common iliac arteries and any artery distal to them as peripheral arteries. By clinical evaluation, we have found only two late postoperative obstructions in the entire group, and many of the cases have been followed for from one to three years. This is in contrast to the report of Warren.[4] Of our two patients having late obstructions, one was operated on three months later because of thrombosis in another portion of his femoral artery and not in the graft. Another graft was successfully placed in his leg, and the pulse in his foot was again restored. The second patient has reverted clinically to her preoperative state, and additional procedures are contemplated.

Among the peripheral aneurysms that were replaced by grafts, three were in the popliteal artery and one in the femoral. The single poor result occurred in a popliteal artery graft. Of the grafts listed under "Trauma," two were for acute injuries in children, one of the popliteal artery and the other of the brachial artery. The latter graft was unsuccessful, since the arm was gangrenous at the time of operation. The remaining graft was used for an arteriovenous fistula of the subclavian vessels after a gunshot wound. The single patient listed under "Tumors" had a pelvic carcinoma that involved an iliac artery, which was removed and successfully replaced. Only readily available grafts make such unexpected procedures possible.

The replacement of diseased, obstructed, or injured major vessels has gained widespread acceptance, and grafting procedures will undoubtedly be done more frequently in the future. The relative merits of homografts versus prostheses are undetermined, and time alone can give us the answer to many of the controversies. It is our opinion that the majority of surgeons today prefer to use a homograft if a suitable one is readily available. The main objection to the use of homografts has been the difficulty of obtaining and preparing them. We believe that, if banks of the type described here were established in most large communities, homografts could be made available throughout the country and their use greatly increased.

Summary

Experience with the operation of an arterial homograft bank at the Hospital of the University of Pennsylvania has shown that procedures requiring use of arterial homografts and maintenance of arterial homograft banks can be provided by large community hospitals without additional highly trained personnel. A bank of arterial homografts increases the scope of treatment of arterial lesions such as arteriosclerosis, tumor, or trauma.

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This study was supported in part by the American Heart Association and the Southeastern Pennsylvania Chapter of the Pennsylvania Heart Association.

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HOW COMMUNICABLE ARE WARTS?

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As early as 1896 Jadassohn[1] pointed out that warts may be transmitted from one person to another. The occurrence and regression of these lesions has furnished a fascinating and abundant stock of folklore. Over many years various and sundry remedies have been recommended for the common wart. Nearly every small community has a "character" possessed of special abilities capable of "bewitching" off warts. For some reason the full moon has become important as a factor assisting in the removal of these lesions. Varied remedies have been suggested by lay persons from a list too long to transmit here. These suggestions often come from people who are otherwise apparently quite intelligent. A complete review of the folklore connected with warts would make a fascinating subject for a treatise. Those of us in dermatology hear these stories almost daily.

• *The distribution of warts was studied in an orphanage where 58 children lived during the winter months. Warts were found in 15. The warts in some instances had been present when the child arrived; in other instances they appeared some time after the child's arrival. There were cases of spontaneous disappearance and subsequent recurrence. The distribution of the lesions on different parts of the body did not afford clues as to the method of dissemination, and the time relations of their appearance were not clear. Four out of 18 adults resident in a seminary cottage reported warts; again it was difficult to interpret the data because information as to the time relations and the distribution among other residents was incomplete. Much work on the transmissibility of these lesions must be done before standard hygienic measures can be established. Better knowledge of this virus infection is very desirable because these lesions are so common. They affected at least 20% of the residents in the seminary cottage and more than 25% of the children in the orphanage.*

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Read before the Section on Dermatology at the 105th Annual Meeting of the American Medical Association, Chicago, June 14, 1956.

Warts as a Virus Infection

Zwick[2] in 1932 made an interesting review of the subject. He states that the principle of physical disease being cured by suggestion is as dramatically presented with warts as with any disease we know. Bloch[2A] postulated an effect through the vegetative nervous system, causing an unfavorable medium for the virus and hence its death. It has been known, for some years now, that warts are a virus infection. This has more recently been pointed out by Strauss and coworkers[3] in their finding of virus-like particles and inclusion bodies in such skin lesions. They were found in some but not all warts. It is generally conceded by those interested in this field that several strains of virus are the etiological agents for various warts. That they are definitely communicable, however, has not been proved. Clinical reports of possible communicability of warts, therefore, would seem in order. There has been a marked paucity of such reports in the literature. The most pertinent one to the group under consideration here is a study by Grigg and Wilhelm[4] in 1953 on the epidemiology of plantar warts among school children. They examined all the children in the public schools of Dixon, Ill., over a period of one year. Of the students, 4.47% were found to have plantar warts. Incidentally, this study was done entirely with plantar warts and no particular study was made of the other types of warts present. As a control Grigg and Wilhelm checked the students in the neighboring village of Amboy, Ill. There they found 0.72% of the children had plantar warts. They felt the percentages were significant enough to be classed as of epidemic proportions. In a fairly carefully worked out comparison they found the following facts: 1. There was no relation to showers or foot baths. 2. Most of the lesions were multiple. 3. Of the warts, 86.7% were at pressure points. 4. Of the total student group, 10.28% had warts elsewhere on their body. 5. There was no difference in the incidence of plantar warts in other members of the family between children with plantar warts and those without plantar warts. Furthermore, Grigg and Wilhelm were unable to isolate a virus from the specimens they examined. These studies were done for them at the University of Michigan, Ann Arbor, Mich.

More recently an editorial[5] has pointed out that, in an examination of 13,000 school children in England, 9.71 children per 1,000 had warts. It is generally known that warts are much more common in girls than boys.[6] In some series,[7] this difference is four to five times as great. This is an interesting observation, for their presence previous to puberty would make it hard to relate to any endocrine activity. One author[5] theorizes that perhaps girls had more contact with bathroom floors than their brothers. Actually the reason for this sex difference is not known. Two-thirds of the cases occur in the age group 11-15.

Observation of Warts

After reviewing the subject and the major pertinent literature, it was deemed worthwhile to report the following group of cases seen in an orphanage over a period of about 18 months. It became apparent that there was an unusual number of patients with warts being brought to the office from this particular orphanage (it is unfortunate that all the inmates are girls). Two of them had been observed with warts several years previously. Twelve patients with warts of various types were observed over an eight-month period. In several other children there was a definite history of warts having been present previous to the ones seen in this present review. Furthermore, one or two of the patients had warts on entering the orphanage; however, by far the majority of them had been contracted after they came there, and no previous warts had been noted in these individuals (see table). Some 58 children are in this orphanage in the winter, while for the summer about 30 remain. Most of them have one parent or are from broken families to whom they can go during the summer when school is not in session. Therefore, the percentage of 25.8% is rough. On the other hand, there probably are several other children in the orphanage who were not seen and who have warts. I have heard this on rumor from some of the children. Furthermore, some of the children who have had warts that have spontaneously disappeared have never been brought in. While a few plantar warts were noted, the majority of the lesions were on other parts of the body, and, in one instance, the only lesion present was on the lip.

*Data on Fifteen Female Patients with Warts in an Orphanage Group**

Age, Yr.	No. of Warts	Location	Date Noted	Duration When Seen
11	8-10	Hands and left foot	2/13/55	2 mo.
15	2	Hand	7/6/55	8 wk. (had warts as child; cleared and recurred)
10	1	Lip	1/12/55	2 mo.
9	1	Palm of hand	7/6/55	4 mo.
13	4	Hand	3/28/55	2 yr.
10	8-10	Hands and leg	7/6/55	4 mo.
6	10-15	Hands and foot	2/13/52	3 mo.
10	1	Plantar on great toe	2/17/54	1 yr.
13	2	Index finger	6/9/55	3 mo.
13	1	Plantar on heel	12/15/53	4 mo.
15	1	Plantar on ball of foot	9/19/53	6 mo.
11	2	Hands	9/55	2 mo.
9	2	Hands	11/20/54	1 yr.
13	4	Hand	6/22/54	1½ yr. (had warts as child; cleared and recurred)
14	1	Thumb	5/10/55	4 mo. (present before entering orphanage)

*Children in orphanage: 58 in the winter and 20 in the summer. Of the winter group, 25.8% were involved.

I have recently observed, over a period of two weeks, three brothers and a priest from the same seminary with warts on their hands. The priest also had several lesions on his feet. The lesions were quite typical and, with one exception, had appeared since they entered the seminary. The first one to have the lesions was the priest. They lived in a cottage of a group of 18.

Comment

How often have we all seen several members of one family with warts? How significant are these findings? I do not think we can pass by the possible communicability of warts of all types. There are many factors known by all of us that point to their method of spread.

For instance, it is well known that combing the hair, shaving, and similar acts definitely transplant the virus, causing new lesions. However, the spread of lesions from one individual to another is a little more difficult to establish. Undoubtedly it does occur. Whether any precautions should be taken in institutions or schools to isolate individuals with warts is another matter. The consensus seems to be that this is not necessary. It may be, however, that, in institutions such as the seminary or orphanage, individuals with warts should observe some precautions. How strict these should be is difficult to say. Certainly a great deal more work must be done on the transmissibility of these lesions before one can establish such standards. It is not my purpose here to try to set up these requirements but merely to point out the possible communicability of this virus infection of the skin that, while similar to the average virus infection in many respects, also has some interesting differences.

Vaccines of wart tissue are ineffective in the therapy of warts. I tried this therapy in a series of cases, some years ago, using both human wart tissue extracts and wart vaccine prepared from the cow. The results were unsuccessful and never published. Veterinarians employ a wart vaccine in the treatment of lesions on cows that I understand is quite successful. Warts on cows apparently are an entirely different virus, with immune reactions equally as different. This merely helps point out the complexity of the problem as well as the lack of knowledge about the spread of one of the commonest of all diseases. There are probably a number of strains of the virus, some of which may be more communicable than others. This has been pointed out by Blank,[6a] and it may well be the explanation of the variability in apparent communicability of these lesions.

Summary and Conclusions

In two groups of institutional residents the incidence of warts was about the same. Of children in a certain orphanage, 25% developed warts over a one and one-half year period. About 20% of the inmates of a small seminary group did the same over a much shorter period. It is felt that some strains of wart virus are more communicable than others, although this has not been proved. Simple precautions may help to prevent the spread of warts.

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BLOOD ASCORBIC ACID LEVEL IN BIOFLAVONOID AND ASCORBIC ACID THERAPY OF COMMON COLD

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• *The incidence and course of common colds were followed in 89 medical students and nurses who volunteered in a study of the efficacy of naringin, a bioflavonoid extracted from grapefruit peel and used in remedies for colds. One group of 22 subjects received 333 mg. of naringin and 65 mg. of ascorbic acid three times daily for three months; a second group received naringin only, another ascorbic acid only, and the fourth a placebo. These substances were administered in capsules as nearly alike as possible. Symptoms of colds were systematically recorded, and the levels of ascorbic acid in the blood were determined periodically. The average level of ascorbic acid in 22 men who were to receive ascorbic acid by mouth was initially 0.96 mg. per 100 cc. of blood; after 12 weeks of taking only ascorbic acid the average for this group was 1.41 mg. per 100 cc. of blood. In all groups and at all stages, the blood ascorbic acid levels for males were significantly lower than those for females. There was no evidence that the naringin affected the ascorbic acid level of the blood, prevented colds, or cured them.*

During the past year treatment with the bioflavonoids has been widely publicized as a means of preventing or modifying the common cold. One of the reasons given for the effect has been that they potentiated ascorbic acid (vitamin C) in alleviating cold symptoms. Since there was no convincing proof available, either in support or in denial, we undertook a pilot study to explore the validity of these statements. Within the limits of this study, the bioflavonoid tested showed effect neither on the incidence or cure of colds nor on the ascorbic acid content of the blood. In the course of the study, interesting data were developed regarding the relationship of blood ascorbic acid levels to the incidence and cure of colds. These are reported in detail.

Method

The study was made on 89 volunteer medical students and student nurses for the three-month period from February to May, 1956. Four groups were established and given capsules (three times daily,

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From the *Dartmouth* Medical School and the Hitchcock Foundation.

orally) made up as follows: group 1, bland placebo, group 2, naringin (bioflavonoid), 333 mg., and ascorbic acid, 65 mg.; group 3, ascorbic acid, 65 mg.; and group 4, naringin (bioflavonoid), 333 mg. (Naringin is an extract of grapefruit peel.) Every effort was made to disguise the contents of the capsules. All looked and tasted alike. Even the doctors conducting the study did not know the key to the code numbers used. Groups were assigned in rotation. Thus the first volunteer in line received bland placebo, the second naringin (bioflavonoid) and ascorbic acid, and the fifth bland placebo, as the rotation started over again.

TABLE 1.—*Blood Ascorbic Acid Level Determinations in Group 1: Patients Given Placebo*

Patient No	Sex	Level, Mg /100 Cc					
		Initial Wk	6th Wk	12th Wk	During Cold	Wk of Cold	Results of Treatment
1	M	1.02	0.60	1.50	0.80	5th	No change
5	M	1.04	1.32	1.60	1.36	5th	Improved
9	M	1.12	1.08	1.52			
13	M	0.72	1.08	1.80	1.24	7th	No change
					1.84	4th	Cured
17	M	1.12	1.12	1.10	1.32	4th	Improved
21	M	0.80	0.76	1.30			
25	M	1.00	1.28	0.88			
29	M	0.40	0.44	0.40			
33	M	1.12	1.16	0.44			
37	F	1.60	1.40	1.28			
41	M	1.16	1.52	1.44			
45	M	1.08	1.12	0.96			
49	M	1.08	1.28	1.10			
53	F	1.60	1.80	.			
57	F	1.20	1.20	...			
61	M	0.76	0.88	1.12			
65	F	1.60	1.16	1.08			
69	F	1.12	1.32	...			
73	F	1.44	1.40	1.40			
77	M	0.44	0.28	0.30	0.40	5th	Worse
81	F	0.52	0.70	1.84	0.80	6th	No change
85	F	1.48	1.64	1.12			
89	M	1.36	.				

TABLE 2.—*Blood Ascorbic Acid Level Determinations in Group 2: Patients Given Bioflavonoid and Ascorbic Acid*

Patient No	Sex	Level, Mg /100 Cc					
		Initial Wk	6th Wk	12th Wk	During Cold	Wk of Cold	Results of Treatment
2	M	1.12	1.48	2.00			
6	M	1.08	1.12	1.48	1.08	2nd	Cured
10	M	0.80	1.16	1.28	0.96	2nd	Cured
					1.16	6th	Worse
14	M	0.96	1.36	1.30			
18	M	1.12	1.60	1.38	1.12	1st	Improved
					1.20	4th	Improved
22	M	0.56	1.52	1.10			
26	M	0.72	1.28	1.20			
30	M	0.72	1.52	...			
34	M	0.96	1.60	1.30			
38	F	1.48	2.00	1.72			
42	M	1.12	1.48	1.30	1.60	4th	Cured
46	M	0.92	1.08	1.04			
50	M	1.08	1.44	1.50			
54	F	1.40	1.84	..			
58	F	1.76	1.84	1.28			
62	F	1.84	1.64	...			
66	F	1.40	1.36	1.72			
70	F	1.88	1.76	1.56			
74	F	1.48	1.44	1.84			
78	M	1.32	1.40	1.84			
82	M	0.96	1.48	...			
86	F	1.28	1.92	1.68			

Each subject received a regional physical examination and had blood taken for a determination of ascorbic acid level the day he started the study. All the volunteers were started on the regimen within a single week. Thereafter they continued taking their particular capsule for the three months of the study. At the 6-week and 12-week points in the study, determinations of blood ascorbic acid level were made on all 89 participants. The subject was instructed to report cold symptoms (such as coryza, headache, malaise, fever, or sore throat) the day of onset. At this time the physical examination and determination of blood ascorbic acid level were repeated. He was asked to take no specific cold remedies, not even aspirin or nasal sprays, during the course of the infection. He continued taking the same dosage of the capsule assigned to his group. No antibiotics were used. During the infection the same physician made a record (daily when possible) of the cold's progress or regression. On the fifth day the cold was evaluated as cured, improved, unchanged, or worse.

Two variables were accepted as calculated risks to the accuracy of the study: diet and individual reliability. Although the majority of the subjects ate in the same hospital cafeteria, precise control of their diet was felt to be beyond the scope of this essentially pilot study. We recognized, of course, the varying degrees of reliability with which 89 persons would take 3 capsules a day for three months; we believe, however, that close supervision and the medical orientation of the participants kept this factor of error at a minimum.

TABLE 3.—*Blood Ascorbic Acid Level Determinations in Group 3: Patients Given Ascorbic Acid*

Patient No	Sex	Level, Mg /100 Cc.					
		Initial Wk	6th Wk	12th Wk	During Cold	Wk. of Cold	Results of Treatment
3	M	1.08	1.32	1.50	1.40	3rd	Improved
7	M	1.28	1.52	2.00	1.92	3rd	Cured
11	M	1.12	1.36	2.00	1.32	3rd	Cured
15	M	0.96	1.68	1.24	1.60	3rd	Improved
19	M	1.12	1.08	0.80	1.08	3rd	Cured
23	M	1.08	1.52	1.10			
27	M	0.72	1.28	1.40			
31	M	1.08	1.16	1.70			
35	M	0.72	0.96	...			
39	F	0.96	. . .	...			
43	M	1.12	1.48	1.20			
47	M	0.76	1.44	1.50			
51	F	1.16	1.28	..			
55	F	2.04	2.08	1.32			
59	F	1.32	1.28	1.20	1.68	1st	Cured
63	F	1.40	1.52	1.84	1.52	4th	Cured
67	F	1.28	1.72				
71	F	1.28	1.40	1.52			
75	F	1.12	1.56	2.72			
79	M	0.88	1.36	1.08	1.52	4th	Improved
83	M	0.96	.	...			
87	M	0.52	...	...			

Tables 1, 2, 3, and 4 give the detailed blood ascorbic acid levels accumulated during this study. They are included in their complete form, partly because they are the basis for the conclusions of this pilot study and partly because comparable records of blood ascorbic acid levels in normal young adults are relatively rare. (Ascorbic acid blood levels were determined according to the technique of Roe and Kuether[1] under the supervision of John P. Davison, Ph.D., assistant professor of the physiological sciences in the Dartmouth Medical School.)

Results

Table 5 summarizes the effectiveness of bioflavonoid with and without ascorbic acid. When used alone, it produced the same results as a placebo. When used with ascorbic acid, the results were comparable to those with ascorbic acid alone. Table 6 indicates that the prolonged administration of bioflavonoid had no effect on the blood ascorbic acid level. Females consistently showed a higher blood ascorbic acid level than males (table 6—statistically significant at the 0.01 level). Most of those receiving ascorbic acid showed an increased blood ascorbic acid level. Those receiving ascorbic acid developed just as many colds as those not receiving it (table 5). In this small series, those receiving ascorbic acid showed more rapid improvement in their colds than those not receiving it (tables 1 to 5 inclusive—statistically significant at the 0.05 level).

Comment

Ascorbic acid deficiencies have been noted not only in classic scurvy but in other infectious and metabolic disorders, such as rheumatoid arthritis, rheumatic fever, tuberculosis, and certain virus infections. The importance of ascorbic acid in maintaining capillary integrity has long been recognized. We will discuss neither the related background nor the literature.

Table 4.—*Blood Ascorbic Acid Level Determinations in Group 4: Patients Given Bioflavonoid*

Patient No.	Sex	Level, Mg./100 Cc. Initial Wk.	6th Wk.	12th Wk.	During Cold	Wk. of Cold	Results of Treatment
4	M	1.20	1.28	1.70	1.28	5th	Cured
8	M	1.08	0.88	1.20			
12	M	0.72	1.20	1.20			
16	M	0.96	0.72	1.00	1.00	5th	Improved
					0.96	1st	Worse
20	M	1.08	1.08	1.00			
24	M	1.00	1.20	0.86			
28	M	1.12	1.08	0.80			
32	M	1.28	1.40	1.00			
36	M	0.88	1.08	1.20	1.00	3rd	Worse
40	M	1.10	0.88	1.30			
44	M	1.08	0.96	1.52	1.08	1st	Improved
48	M	1.28	0.70	1.20			
52	F	1.08	1.20	1.28	1.12	7th	Improved
56	F	1.75	1.64	...			
60	F	1.56	1.18	1.32	1.08	3rd	Improved
					1.20	5th	Worse
64	F	1.56	1.40	1.44			
68	F	1.80	1.84	1.60			
72	F	1.48	...	...			
76	F	1.72	1.84	...			
80	M	0.64	0.96	0.60			
84	F	1.24	...	...			
88	F	1.36	1.48	1.50			

Recently certain naturally occurring substances have been found to have a related function in maintaining the integrity of the intercellular cement substance. The materials as a group have been classified as flavone glycosides and include such substances as hesperidin, rutin, and naringin. We are particularly concerned with those substances derived from citrus fruit peels, grouped together under the title of bioflavonoids. The significant literature on this subject was summarized at a meeting of the New York Academy of Sciences in 1955, which is reported in the annals of that organization.[2] Various articles in this monograph suggest a relationship between ascorbic acid and the bioflavonoids, with particular reference to their effects on capillary fragility. The monograph also reports the clinical use of the bioflavonoids and ascorbic acid in the treatment of disorders related to decreased capillary permeability. These include poliomyelitis, rheumatic fever, and bleeding related to pregnancy. The hypothesis that the bioflavonoids may prevent or modify colds is apparently based on this same property.

With this possibility in view, a number of drug compounds appeared on the market during the winter of 1955-1956 featuring a bioflavonoid content. Most of these compounds also contained such old cold treatment stand-bys as aspirin, caffeine, and ascorbic acid. The limited statements regarding this treatment of colds reported the use of the whole compound, without reference to specific studies based on the effect of the bioflavonoid alone.

We are reporting a pilot study on the effectiveness of one bioflavonoid per se. It is, of course, not definitive. But, in the absence of any comparable evaluation of a material whose commercial distribution is already widespread, we feel that even this limited study may be helpful to the medical profession. The approximately 300 determinations of blood ascorbic acid level were a by-product of the bioflavonoid study. The series is far too small to warrant conclusive interpretations, but the data raise several points of interest that may serve as points of departure in more definitive studies.

Table 5.—*Incidence and Cure of Colds with Bioflavonoid and Ascorbic Acid*

Group	No. in Group	No. Colds in Group	Colds Cured or Improved in 5 Days
Placebo	23	7	3
Bioflavonoid plus ascorbic acid	22	6	5
Ascorbic acid	22	8	8
Bioflavonoid	22	8	4

Table 6.—*Average Blood Ascorbic Acid Level in Males and Females*

	Level, Mg./100 Cc. Placebo		Bioflavonoid Only		Ascorbic Acid Only		Bioflavonoid and Ascorbic Acid	
	M	F	M	F	M	F	M	F
Initial	0.95	1.32	1.06	1.48	0.96	1.32	0.96	1.56
6th wk.	0.99	1.33	1.04	1.55	1.35	1.55	1.39	1.76
12th wk.	1.12	1.28	1.12	1.43	1.41	1.72	1.39	1.63

Summary

We are reporting a controlled pilot study of the clinical effect of bioflavonoids and ascorbic acid (vitamin C) on the incidence and cure of the common cold, correlated with serial determinations of blood ascorbic acid level on the 89 medical students and student nurses comprising the test group. The administration of a bioflavonoid had effect neither on the incidence or cure of colds nor on the ascorbic acid level of the blood.

This study was supported by grants from the Nepera Chemical Co., Inc., Yonkers, N. Y., and the Harriet M. Spaulding Charitable Trust.

Statistical analyses were done by J. Laurie Snell, assistant professor of mathematics, Dartmouth College.

All drug preparations were provided by the Nepera Chemical Co., Inc.

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USEFULNESS OF BIOFLAVONOIDS AND ASCORBIC ACID IN TREATMENT OF COMMON COLD

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• *The evaluation of any drug used to treat the common cold must necessarily be based on clinical observations. Bioflavonoids and ascorbic acid, singly and in combination, were evaluated in a study on almost 2,000 persons as to their efficacy, not by symptom alleviation but as to whether it would shorten the course of illness. The overwhelming impression gained from the study presented is the singular lack of effect in altering the course of the common cold by either the bioflavonoid or the ascorbic acid.*

The objective evaluation of a new form of treatment for the common cold has always proved difficult. Since the viruses causing it have thus far completely resisted all attempts at direct annihilation through the use of antibiotics, no bacteriological studies on the disappearance of the causative organism have proved feasible, nor have any other laboratory tests been found of great use in estimating the individual's rate of recovery. Therefore, the evaluation necessarily has been based essentially on clinical observations.

Basically, treatment of the common cold has been limited to the relief of symptoms, the prevention of complications, and the general and specific supportive therapies that enable the body's own defense mechanisms to overcome the disease. Because the illness is essentially self-limited, with serious complications developing in only a small proportion of cases, any therapy that alleviates the patient's symptoms is called a cure until the test of time reduces it to the level of the other drugs that make the patient more comfortable but do not appreciably affect the underlying cause of the disease. To postulate that a given drug has a specific effect upon the disease, therefore, it must be shown that it does more than relieve symptoms. It should shorten the course of the illness. Furthermore, since there are innumerable drugs that make the patient more comfortable and alleviate symptoms, thereby creating subjective evidence that they are affecting the course of the cold, a cold cure should have an effect over and above the best of these relief medications. Lastly, in view of the fact that the evaluation of effect is almost entirely clinical, and therefore subjective from the point of view of either the patient or the observer, the beneficial result of the drug should be demonstrable in a controlled experiment in which personal bias has been entirely eliminated.

In the past decade, much attention has been given to the treatment of colds by the use of drugs that would enhance the body tissue's resistance to invasion. This has been at least in part behind the rationale for the use of such agents as antihistamines.[1] Even more recently, the administration of ascorbic acid (vitamin C) has been advocated,[2] both to raise the general resistance and on the theory that viral invasion is a function of capillary wall permeability that could be reduced by raising the ascorbic acid levels in the blood. On the basis of this theory, ascorbic acid has been added to a number of preparations used for the treatment of acute upper respiratory infections. The most recent approach to the problem has been an extension of this theory. It has been noted that the citrus bioflavonoids enhance the effect of ascorbic acid in maintaining or restoring to normal the integrity of the capillary wall.[3] In particular, they have been reported as directly combating virus infections by preventing the micro-organisms from penetrating the capillary endothelium.[4] It has been logically argued, therefore, that the bioflavonoids can exert a beneficial effect on the body's ability to resist the invasion of respiratory viruses, and several observers have reported cases that appear to substantiate this claim.[4] Because of the widespread interest in this attack on the problem of the common cold, it was felt that a definitive test of these agents would be of considerable value.

Since it is admitted that neither ascorbic acid nor the bioflavonoids have any in vitro effect on respiratory viruses,[7] such a study would have to be entirely clinical. It would be necessary to prove either that an appreciable number of colds were aborted in their early stages or that some or all of the symptoms were cleared up significantly earlier. The effect looked for would be more than a temporary alleviation of symptoms and should therefore be demonstrable even in the presence of other medicaments given merely to that end. To avoid any possibility of observer bias, the trials should be made on a completely blind basis.

Methodology

Since the bioflavonoids were postulated as acting in conjunction with ascorbic acid, it was felt necessary to study the effect of the two substances both singly and in combination. An experimental design was used that would permit the evaluation of each compound independently and also would demonstrate any synergistic effect obtained. The trials were therefore conducted with the following four preparations: (1) 250 mg. of bioflavonoid (lemon bioflavonoid complex 497, Sunkist Growers) plus 50 mg. of ascorbic acid; (2) 250 mg. of bioflavonoid; (3) 50 mg. of ascorbic acid; and (4) placebo.

The subjects were divided into four groups, each of which was given one of these preparations four times a day. In order to demonstrate that any effect ob-

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Medical Director, Sylvania Electric Products, Inc. (Dr. Tebrock) and Medical Director, Pratt-Whitney and Company, Inc., West Hartford, Conn. (Dr. Johnston).

served was more than that obtainable through standard palliative practice, every patient received a preparation containing 325 mg. of salicylamide, 195 mg. of acetophenetidin, 65 mg. of caffeine, and 50 mg. of thonzylamine hydrochloride. This was done so that a patient not receiving ascorbic acid or bioflavonoid or a combination was actually receiving medication, which, in addition, acted as a control.

Table 1.—*Comparison of Eight Test Groups for Randomness of Distribution*

	Group 1 Without Flavonoid or Ascorbic Acid		Group 2 With Flavonoid and Ascorbic Acid		Group 3 Without Flavonoid and With Ascorbic Acid		Group 4 With Flavonoid and Without Ascorbic Acid		Group 5 Without Flavonoid or Ascorbic Acid		Group 6 With Flavonoid and Ascorbic Acid		Group 7 With Flavonoid and Without Ascorbic Acid		Group 8 Without Flavonoid and With Ascorbic Acid	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Sex																
Male	134	53.2	138	60.3	144	55.2	134	54.9	129	54.0	136	55.7	122	49.8	126	52.5
Female	118	46.8	91	39.7	117	44.8	110	45.1	110	46.0	108	44.3	123	50.2	114	47.5
Total	252		229		261		244		239		244		245		240	
Ages																
Up to 20	13		11		10		16		11		7		13		18	
21-25	38		47		37		45		49		49		41		42	
26-30	47		49		67		57		60		70		62		50	
31-35	64		48		45		46		44		41		44		57	
36-40	32		27		44		34		24		24		32		25	
41-45	26		17		32		23		22		23		31		20	
46-50	13		8		8		10		12		9		10		10	
51-55	10		5		8		9		7		14		4		8	
56 +	4		9		8		2		6		4		5		7	
Total	247		221		259		242		234		241		242		237	
Mean age	34.0		33.0		34.2		32.8		32.8		33.2		33.2		33.0	
Mean no. of colds per yr.	2.65		2.72		2.72		2.78		2.53		2.51		2.99		2.54	

Use of these four preparations enables one, by means of a square experimental design, to simultaneously compare the effect of two drugs, both separately and together, and yet to use all the patients in each of the comparisons. In figure 1, each of the boxes represents an approximately equal number of patients receiving the drugs indicated. The effect of ascorbic acid (A in fig. 1) could be evaluated by comparing the upper two boxes and that of bioflavonoid (B in fig. 1) could be evaluated by comparing the two left-hand ones, but this would utilize only half the patients for each evaluation. If, however, the patients in the left-hand side of the square are compared with those in the right-hand half, the effect of ascorbic acid will be demonstrated using all the patients, since the two halves represent the same distribution except for the presence or absence of this factor. The patients indicated in the lower box of each half also receive bioflavonoid, but, since they are about the same proportion of the total, the effect of the latter will cancel out unless a marked synergism is present. The difference produced by bioflavonoid, irrespective of ascorbic acid, can be shown similarly by comparing the upper and lower halves. The amount of synergism or antagonism can be evaluated by determining whether the difference between OO (placebo) and AB is significantly greater or less than the sum of the difference between OO and AO plus OO and OB.

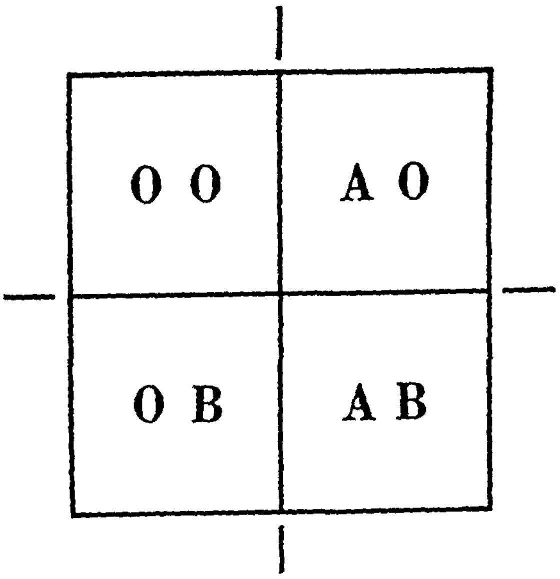

Fig. 1.—Diagram of square experimental design. O = placebo; A = ascorbic acid; and B = bioflavonoid.

The trials were conducted on subjects reporting to several outpatient industrial clinics under the supervision of the physicians conducting the study. A number of college, seminary, and private patients of one of the authors were also included. Medicaments supplied to these physicians were identified only by number, so that neither they nor the patients were aware of what was being given. Furthermore, in order to reduce the possibility of the clinical judgments being influenced by continued association of better results with one of the preparations, each of them was supplied under two numbers, making eight test groups in all to which the patients were assigned in rotation.

Table 2.—*Additional Diagnoses and Other Medications in Drug Groups*

	Flavonoid				Ascorbic Acid			
	With		Without		With		Without	
Additional Diagnoses	No.	%	No.	%	No.	%	No.	%
Pharyngotonsillitis	61	6.4	66	6.8	64	6.7	63	6.6
Tracheobronchitis	42	4.4	37	3.8	42	4.4	37	3.9
Antibiotic given	69	7.3	63	6.5	71	7.4	61	6.4
Nasal decongestant	135	14.2	133	13.7	133	13.9	135	14.1
Cough medicine	89	9.4	116	12.0	92	9.6	113	11.8
Pills not all taken	221	23.3	200	20.6	222	23.2	199	20.7
Total in group	947		969		956		960	

Because it was not feasible to reexamine the subjects daily, a single checkup after three days was decided on. It was felt that, if colds were aborted to any appreciable degree by one or both of the drugs, the number of cures after three days should be appreciably higher than in the controls. At the same time, while some alleviation of symptoms was expected in all groups, the proportion should be materially increased in any group receiving an effective therapeutic agent in addition to the palliative medicament. The three-day limit was selected because, with a longer interval, too many cases might resolve spontaneously, while a shorter time would not afford a chance for disappearance of symptoms even under effective therapy. Since the dispensaries were in operation from Monday through Friday, only those cases first seen on Monday, Tuesday, and Friday were included in the study, in order to permit a return at the proper time.

Patients coming to the dispensaries or private offices on those days were first examined. If a diagnosis of an acute upper respiratory infection was made, patients were admitted to the study and assigned to one of the eight test groups in sequence. Their symptoms, physical findings, and other pertinent data were then recorded on a special printed form, which was precoded for machine punching and tabulation. The patient was given sufficient medicament to provide four doses a day for three days and instructed to report back at the end of that time. To simplify compounding and dispensing the medicaments, the ingredients that varied from group to group were put into one capsule, while those given to all groups were put in another. Cough medicine and nasal decongestants were also dispensed if indicated and were recorded on the form. In the case of the industrial patient, when secondary bacterial infection appeared to be developing, he was recommended to his personal physician.

Symptoms to be recorded were limited to eight considered most characteristic of the common cold: running nose, sneezing, hoarseness, cough, malaise, headache, postnasal drip, and sore throat. Only their presence or absence at the initial visit was noted, to avoid the difficulty of grading their severity. The time since the onset of the first symptoms was also recorded, as was the patient's temperature at the initial visit. The notation of physical findings was also limited to those associated with acute upper respiratory infections. Nasal secretions were reported as none, slight or marked, or mucoid or purulent and nasal obstruction as none, partial or complete, or unilateral or bilateral. Pharyngitis was graded as none, mild, moderate, or severe. The diagnoses of pharyngotonsillitis or tracheobronchitis were recorded if present.

TABLE 3.—*Subjective and Objective Change by Drug Groups*

	Bioflavonoid				Ascorbic Acid			
	With		Without		With		Without	
Change	No.	%	No	%	No	%	No.	%
Subjective								
Worse	110	11.7	122	12.5	111	11 6	121	12 6
No change	218	23.1	217	22 3	225	23 5	210	21.9
Improved	406	43.1	400	41.1	409	42.7	397	41.5
Cured	208	22 1	234	24 0	213	22 2	229	23 9
Total	942		973		958		957	
Objective								
Worse	79	8 4	93	9 6	85	8 9	87	9.1
No change	200	21.3	189	19.5	201	21.2	188	19 6
Improved	441	47 0	449	46.2	443	46 6	447	46 6
Cured	218	23 2	240	24.7	221	23.3	237	24.7
Total	938		971		950		959	

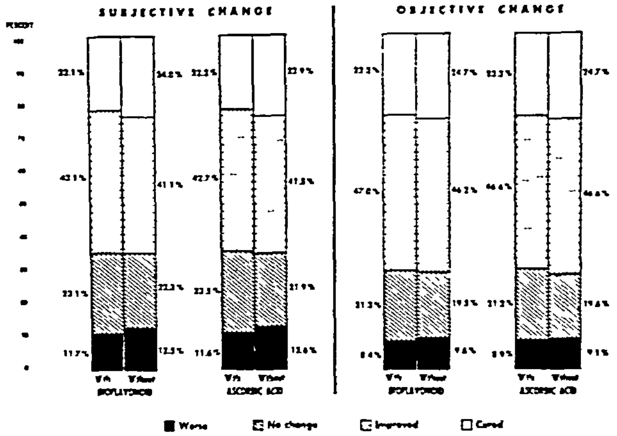

Fig. 2.—Subjective and objective change by drug groups.

At the examination on the third day, the presence or absence of the same symptoms was again recorded, and the physical findings were graded as before. The over-all change in the patient was evaluated, both subjectively and objectively, as worse, no change, improved, or cured. A note was made on whether the patient had taken all his pills and whether he had remained at work and on the number of days lost, if any. All these entries could be recorded on the study form simply by circling the appropriate finding under each heading.

Analysis of Results

Almost 2,000 individuals with acute upper respiratory infections between January and May, 1956, were used in the study. A small number were dropped for failure to report back on the third day, and a few study forms were not completely filled out, but the over 1,900 observations reported under all headings were a more than adequate sample to demonstrate any significant differences that might be produced by the drugs. The coded findings on each case were punched on IBM cards, which were then sorted by test group. These were tabulated for each observation and the distributions percentaged or converted to means. (Where appreciable differences in percentages or means were found, tests for statistical significance were made, using a chi-square test for percentage variations and a t-test for evaluating differences in means. Because of the many observations compared, differences were not considered significant unless the chance probability was 1% or less.)

Table 1 shows the distribution of the eight treatment groups by age and sex. The small differences noted were all accounted for by random sampling variation, and there were no statistically significant differences. The comparability of mean number of colds per year shown in this table indicates that the groups were also random with regard to patients' susceptibility to colds. These eight groups were com-

TABLE 4.—*Decrease in Symptoms by Drug Groups*

Symptoms	Total Patients	Present Initially No.	Present Initially %	After 3 Days	Decrease, %	Total Patients	Present Initially No.	Present Initially %	After 3 Days	Decrease, %	Difference in % Due to Drug
	With Flavonoid					Without Flavonoid					
Running nose	917	621	67.7	330	46.9	969	659	68.0	334	49.3	—2.4
Sneezing	917	534	58.2	165	69.1	969	579	59.8	156	73.1	—4.0
Hoarseness	945	352	37.2	163	53.7	982	386	39.3	181	53.1	0
Cough	945	406	43.0	320	21.2	982	463	47.1	348	24.8	—3.6
Malaise	929	444	47.8	160	64.0	962	493	51.2	166	66.3	—2.3
Headache	929	447	48.1	172	61.5	962	491	51.0	173	64.8	—3.3
Postnasal drip	949	325	34.2	193	40.6	979	316	32.3	186	41.1	—0.5
Sore throat	949	455	47.9	188	58.7	979	447	45.7	186	58.4	+0.3
	With Ascorbic Acid					Without Ascorbic Acid					
Running nose	936	640	68.4	339	47.0	950	640	67.4	325	49.2	—2.2
Sneezing	936	570	60.9	161	71.8	950	543	57.2	160	70.5	+1.3
Hoarseness	961	371	38.6	175	52.8	966	367	38.0	169	54.0	—1.2
Cough	961	432	45.0	329	23.9	966	437	45.2	339	22.4	+1.5
Malaise	941	441	47.0	145	67.3	947	493	52.1	181	63.3	+4.0
Headache	944	464	49.2	182	60.8	947	474	50.1	163	65.6	—4.8
Postnasal drip	958	335	35.0	201	40.0	970	306	31.5	178	41.8	—1.8
Sore throat	958	440	45.9	185	58.0	970	462	47.6	189	59.1	—1.1

bined into two groups representing the patients receiving and not receiving bioflavonoids, and also the two different groups that did and did not receive ascorbic acid. The following tabulations are presented for all these combinations. Table 2 gives further evidence of the statistical comparability of the groups. The percentage of patients with pharyngotonsillitis and tracheobronchitis was not significantly different from group to group. Roughly the same proportion of patients required additional medicaments in each group, including antibiotics, nasal decongestants, and cough medicine, in addition to the medicaments under test, and none of these additional medicaments was given in a high enough percentage of cases to have seriously influenced the results of the study. The proportion of patients who did not take all their pills also did not vary significantly between groups. Cross tabulations (not shown) of all these factors against subjective and objective improvement indicated that the elimination of patients who received supplementary medicaments or did not take all their pills would not have appreciably affected the results of the study.

Table 3 shows the effect of bioflavonoid and ascorbic acid on the improvement after three days, judged by both the patient and the clinician. The distributions with and without each of the drugs are almost identical, for both subjective and objective change, with absolutely no statistically significant differences demonstrable. This is graphically illustrated in figure 2. The ameliorating effects of the two drugs on the patients' symptoms are evaluated in table 4. It will be noted that on initial examination the percentage of patients in each group having each symptom was strictly comparable. The number of patients having the symptoms at the end of three days was then tabulated, and the percentage decrease, based on the number originally reported, was calculated. In a few instances patients developed symptoms after the first visit, but these cases were canceled by others in which the symptoms disappeared, and the number in any event was too small to affect the statistical significance of the data. The difference in percentage decrease that might be attributable to drug effect is shown in the right-hand column. It clearly indicates that neither bioflavonoid nor ascorbic acid had more than a random effect on any of the symptoms of the patients.

The effect of the two drugs on nasal secretions is shown in table 5. Again the initial distributions are well within random limits. There is a noticeable drop in the percentage with mucoid secretions after three days, but this change is almost identical in the groups receiving and not receiving both bioflavonoid and ascorbic acid. There is an actual increase in the per-

TABLE 5.—*Change in Nasal Secretions by Drug Groups*

Nasal Secretion	Initial No.	Initial %	Three Day No.	Three Day %	Change, %	Initial No.	Initial %	Three Day No.	Three Day %	Change, %
	With Flavonoid					Without Flavonoid				
None	281	30.3	462	49.9	+64.4	286	29.7	482	50.1	+68.5
Slight mucoid	442	47.7	297	32.1	—32.8	459	47.7	326	33.9	—29.0
Marked mucoid	142	15.3	85	9.2	—40.1	164	17.0	79	8.2	—51.8
Slight purulent	42	4.5	46	5.0	+ 9.5	27	2.8	34	3.5	+25.9
Marked purulent	19	2.1	36	3.9	+89.5	26	2.7	41	4.3	+57.7
Total	926		926			926		926		
	With Ascorbic Acid					Without Ascorbic Acid				
None	278	29.5	459	48.7	+65.1	289	30.6	485	51.3	+67.8
Slight mucoid	448	47.5	314	33.3	—29.9	453	47.9	309	32.7	—31.8
Marked mucoid	154	16.3	75	8.0	—51.3	152	16.1	89	9.4	—41.4
Slight purulent	35	3.7	44	4.7	+25.7	34	3.6	36	3.8	+ 5.9
Marked purulent	28	3.0	51	5.4	+82.1	17	1.8	26	2.8	+52.9
Total	943		943			945		945		

TABLE 6.—*Decrease in Nasal Obstruction by Drug Groups*

Nasal Obstruction	Initial No	Initial %	Three Day No	Three Day %	Change, %	Initial No.	Initial %	Three Day No	Three Day %	Change, %
	With Flavonoid					Without Flavonoid				
None	570	59.7	705	73.9	—14.2	581	59.6	756	77.5	+17.9
Partial, one side	164	17.2	126	13.2	— 4.0	177	18.2	118	12.1	— 6.1
Partial, both sides	173	18.1	100	10.5	— 7.6	172	17.6	81	8.3	— 9.3
Complete, one side	19	2.0	9	0.9	— 1.1	17	1.7	6	0.6	— 1.1
Complete, both sides	28	2.9	14	1.5	— 1.4	28	2.9	14	1.4	— 1.5
Total	954		954			975		975		
	With Ascorbic Acid					Without Ascorbic Acid				
None	569	59.2	726	75.5	+16.3	582	60.1	735	75.9	+15.8
Partial, one side	171	17.8	124	12.9	— 4.9	170	17.6	120	12.4	— 5.2
Partial, both sides	170	17.7	84	8.7	— 9.0	175	18.1	97	10.0	— 8.1
Complete, one side	19	2.0	9	0.9	— 1.1	17	1.8	6	0.6	— 1.2
Complete, both sides	32	3.3	18	1.9	— 1.4	24	2.5	10	1.0	— 1.5
Total	961		961			968		968		

centage of patients having purulent nasal discharges, probably representing the development of secondary bacterial infection, but once more no significant effect on this phenomenon can be attributed to the drugs being tested. The changes in nasal obstruction in the course of the respiratory diseases are tabulated in table 6. The distribution by degree of obstruction was almost identical before treatment in the test groups. There was a uniform decrease in the amount of obstruction in all groups, with no significant differences attributable to either of the drugs.

In table 7, the amount and severity of the pharyngitis found is tabulated. Again there were no appreciable differences in the distributions before therapy. There was a uniform decrease in the amount of pharyngitis found after three days, with neither of the changes in distribution exhibiting more than random variation.

Although this study was designed for outpatient follow-up, it was felt that the disposition and lost time might shed some light on the function of the drugs. Table 8 indicates that there has been no effect on these factors. The proportion of subjects sent home from work on the first visit could not be attributed to drug effect, but the uniformity noted is another indication of the comparability of the groups with regard to severity of infection. The percentage sent home on a subsequent visit might be an inverse index of the efficacy of the medication, but again there was no appreciable variation. The mean number of days lost, which would be a function of both initial severity and drug effectiveness, also showed no statistically significant differences.

On the theory that the effect of the drugs on capillary permeability might only be beneficial if they were given at the start of the illness, the data on patients treated within 24 hours of the development of symptoms were sorted out and tabulated in table 9 for subjective and objective change after three days. Not only was no difference of effect noticed between the patients who did or did not receive either of the drugs, but the distribution by improvement did not differ significantly from that in the total number of patients, regardless of the number of days since onset (table 3).

Since the study was conducted in the dispensaries or offices under the supervision of three different physicians, it was considered advisable to evaluate some of the findings in each separately, to determine whether any had achieved significantly different results than the others. This analysis for subjective change is shown in table 10. It will be noted that the distributions are noticeably different under the three auspices, with statistical significance at well beyond the 0.1% level between all of them. This is due either to variation among the institutions in the standards for determining the subjective changes or to factors in the composition of the groups or the collateral treatment, such as the inclusion of students and private patients. The locality and the infecting organism may also be a factor. It is interesting, also, that all areas of the United States were included in this study. That it was not due to either bioflavonoid or ascorbic acid is evident from the fact that, despite wide variation in distribution between institutional groups, there were no statistically significant differences due

TABLE 7.—*Decrease in Pharyngitis by Drug Groups*

Pharyngitis	Initial No	Initial %	Three Day No	Three Day %	Change, %	Initial No	Initial %	Three Day No	Three Day %	Change, %
	With Flavonoid					Without Flavonoid				
None	530	57.7	703	76.6	+18.9	531	56.3	730	77.4	+21.1
Mild	302	32.9	175	19.1	—13.8	321	34.0	171	18.1	—15.9
Moderate	71	7.7	32	3.5	— 4.2	72	7.6	31	3.3	— 4.3
Severe	15	1.6	8	0.9	— 0.7	19	2.0	11	1.2	— 0.8
Total	918		918			943		943		
	With Ascorbic Acid					Without Ascorbic Acid				
None	530	57.0	721	77.6	+20.6	531	57.0	712	76.4	—19.4
Mild	318	34.2	167	18.0	—16.2	305	32.7	179	19.2	—13.5
Moderate	62	6.7	33	3.6	— 3.1	81	8.7	30	3.2	— 5.5
Severe	19	2.0	8	0.9	— 1.1	15	1.6	11	1.2	— 0.4
Total	929		929			932		932		

to the two drugs within any of the groups. The percentage differences noted, particularly in the Pratt-Whitney group, are still within the limits of random variation for a group of this size.

When the study had been running for several months, a preliminary check on the cases already reported indicated no effect from the bioflavonoids. On the off chance that another compound might prove more effective, the medicaments were switched from lemon to orange flavonoid and the study continued. The difference in effect of these two products on subjective and objective change is shown in table 11. While the lack of effect is more evident in the lemon flavonoid group, the differences noted between the patients receiving and not receiving orange flavonoid did not reach statistical significance and can be completely accounted for by chance variation. It will be noted that the results with orange flavonoid were significantly worse than those obtained with the lemon flavonoid controls. This difference is probably due to a change in the severity of respiratory disease in the later months when the orange compound was being evaluated and emphasizes the importance of simultaneous controls as were used in this study.

TABLE 8.—*Disposition of Cases and Mean Number of Work Days Lost by Drug Groups*

	Bioflavonoid				Ascorbic Acid			
	With		Without		With		Without	
Disposition of cases	No.	%	No.	%	No.	%	No.	%
Kept at work	806	87.4	821	87.3	824	88.4	806	86.3
Sent home after first visit	76	8.2	83	8.8	72	7.7	87	9.3
Sent home on subsequent visit	40	4.3	37	3.9	36	3.9	41	4.4
Total	922		941		932		934	
Mean no. of work days lost	1.174		1.105		1.091		1.181	

TABLE 10.—*Subjective Change by Study Groups*

	Tebrock				Arminio				Johnston			
	With		Without		With		Without		With		Without	
Change	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Flavonoid												
Worse	91	12.7	103	13.9	0	0	1	0.9	21	17.6	15	13.3
None	155	21.6	145	19.6	35	32.1	29	25.4	30	25.2	42	37.2
Improved	307	42.8	303	40.9	46	42.2	54	47.4	54	45.4	44	38.9
Cured	165	23.0	190	25.6	28	25.7	30	26.3	14	11.8	12	10.6
Total	718		741		109		114		119		113	
Ascorbic Acid												
Worse	93	12.7	101	13.9	0	0	1	0.9	15	12.9	21	18.1
None	143	19.6	157	21.5	35	32.1	29	25.4	47	40.5	25	21.6
Improved	322	44.1	288	39.5	47	43.1	53	46.5	41	35.3	57	49.1
Cured	172	23.6	183	25.1	27	24.8	31	27.2	13	11.2	13	11.2
Total	730		729		109		114		116		116	

Comment

The overwhelming impression gained from all these data is the singular lack of effect produced by either the bioflavonoid or the ascorbic acid. If any real clinical response were produced by either of these drugs in even an appreciable minority of the patients treated with them, significant statistical differences should have been evident in at least some of the factors observed. This is particularly so because of the large sample size and the exact comparability of the test groups for all observed factors at the start.

The lack of difference cannot be attributed to the limitation to a single reobservation. In any drug influencing the course of an acute self-limited disease, some changes must be noticeable in at least some of the symptoms after three days or else the effect is so negligible that it can be completely discounted. The procedure used did not evaluate the effectiveness of either of the drugs in preventing secondary bacterial infections and other complications, for which a minimum of a second reexamination after one week would have been necessary, because it had been designed to test the claim that the bioflavonoids, in conjunction with ascorbic acid, aborted or cured the common cold. Neither did it evaluate the use of these vitamins in prophylaxis against the common cold.

TABLE 9.—*Subjective and Objective Change in Patients Treated in First Twenty-four Hours by Drug Groups*

	Flavonoid				Ascorbic Acid			
	With		Without		With		Without	
Change	No.	%	No.	%	No.	%	No.	%
Subjective								
Worse	65	11.2	61	11.5	62	11.1	64	11.6
None	125	21.6	113	21.3	122	21.8	116	21.1
Improved	241	41.6	215	40.5	236	42.1	220	40.0
Cured	148	25.6	142	26.7	140	25.0	150	27.3
Total	579		531		560		550	
Objective								
Worse	41	7.4	49	9.4	46	8.5	44	8.2
None	112	20.1	87	16.7	100	18.4	99	18.5
Improved	253	45.4	239	45.8	254	46.7	238	44.5
Cured	151	27.1	147	28.2	144	26.5	154	28.8
Total	557		522		544		535	

The study cannot be invalidated on the basis of too high a percentage of placebo reactors. It is well known that the majority of common colds are alleviated to some extent by the administration of any symptomatic therapy, and the improvement noted in the over 1,900 cases is about what one would expect after three days of such therapy. For the claims for the drugs being tested to be substantiated, there would have to have been present an effect over and above that found for the entire group, and this difference was completely lacking.

It will be noted that no analyses were performed on the individual drug groups to evaluate synergism or antagonism. In the absence of any differences between the combined groups specific for bioflavonoid and for ascorbic acid (see section on methodology), it seemed necessary to look for such effects. It is statistically possible for two drugs to both have a beneficial effect but to be completely antagonistic and cancel each other, in which case the analysis used would yield a false-negative result. An unusual effect of this kind, however, would be immediately apparent by simple inspection of the data at the time the groups were combined, and it was not noted.

TABLE 11.—*Difference Between Lemon and Orange Flavonoid*

	Lemon				Orange			
	With		Without		With		Without	
Change	No.	%	No.	%	No.	%	No.	%
Subjective								
Worse	102	12.6	101	12.3	10	7.4	18	12.1
None	171	21.1	157	19.2	49	36.3	59	39.6
Improved	353	43.5	342	41.8	54	40.0	59	39.6
Cured	185	22.8	219	26.7	22	16.3	13	8.7
Total	811		819		135		149	
Objective								
Worse	68	8.8	72	9.0	5	3.8	15	10.3
None	154	19.8	145	18.1	41	31.1	39	26.7
Improved	369	47.5	368	45.9	60	45.5	75	51.4
Cured	186	23.9	216	27.0	26	19.7	17	11.6
Total	777		801		132		146	

Thus far there is no convincing evidence that bioflavonoids or ascorbic acid can alleviate a cold when used alone or in combination with other therapies, and our evidence confirms the conviction that bioflavonoids or ascorbic acid are without specific effect in such conditions. Although some might argue that much higher doses of either bioflavonoids or ascorbic acid are necessary to demonstrate a curative effect, we emphasize that the patients in this study received 200 mg. of ascorbic acid and 1 gm. of bioflavonoid per day, levels generally considered adequate to affect the capillary permeability. Since the usefulness of these compounds in reducing capillary fragility has generally been applied to long-standing conditions, there is no reason to believe that massive doses would achieve the rapid effect necessary in conditions as acute as a cold.

Summary

The effect of 1 gm. of bioflavonoid and/or 200 mg. of ascorbic acid administered daily in aborting or curing the common cold was tested in a controlled double-blind trial on over 1,900 subjects. The medicaments were given, either singly or in combination, in addition to the usual treatment used to alleviate symptoms. No appreciable effects were observed after three days on subjective or objective improvement; on disappearance of running nose, sneezing, cough, hoarseness, malaise, headache, postnasal drip, or sore throat; on decrease in nasal secretions or obstruction or pharyngitis; or in time lost from work. In our opinion neither of these drugs in the dosage given has any significant effect in altering the course of the common cold.

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The following doctors from the staff of Sylvania Electric Products, Inc., recorded and commented on the clinical observations used in this study: William Young, Hilton Lopez, Manuel Kaufman, Thomas Foote, C. Stafford Clay, William H. Regelman, Russell Pfeil, Jerome Paparella, Charles Youngman, S. C. Bower, George Means, S. Gardner, Edwin Reynolds, Cornelius Driscoll, Emil Bove, Charles Fleck, Paul Gallaher, Carl Lohmann, Joseph Zavisca, George Cody, and Quay McCune.

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CLINICAL NOTES

A SIMPLE AID IN CALCULATION OF DIETS

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In the construction of diets for alteration of the body weight of adults, certain assumptions have long been employed. Though not entirely accurate, they have the merit of utility and may be stated briefly as follows: 1. For every individual there exists an "ideal" body weight, which may be calculated by a rule of 110 lb. (49.9 kg.) for a person 5 ft. (152.4 cm.) tall, with 5 lb. (2.3 kg.) added for each additional inch. It is customary to allow a variation of 10% in this value, depending on body build. 2. A person who is mainly sedentary requires a daily dietary allowance of 35 calories per kilogram of body weight. If he eats 35 calories per kilogram of his ideal weight, his actual weight, regardless of what it is, will remain constant. If he does heavy labor, however, his caloric requirement may be as high as 40 or 50 calories per kilogram per day. 3. If a person eats more than 35 calories per kilogram of his ideal weight per day, he will gain weight at the rate of 1 gm. of fat plus 1 gm. of water for each 9 calories in excess. If he eats less than the ideal amount, he will lose correspondingly.

These assumptions, admittedly only approximately correct, may be used for calculating weight-changing diets, as in this example. An office worker who is 5ft. 6 in. (167.6 cm.) tall wishes to lose 11 lb. (5.0 kg.) in a month. The required diet is found from the following computations: (1) 11 lb. = 5 kg. = 5,000 gm.; (2) 5,000 gm. ÷ 30 days = 166 gm. per day, equivalent to 83 gm. of fat plus 83 gm. of water per day; (3) 83 gm. of fat is the equivalent of 83 × 9, or 747 calories less

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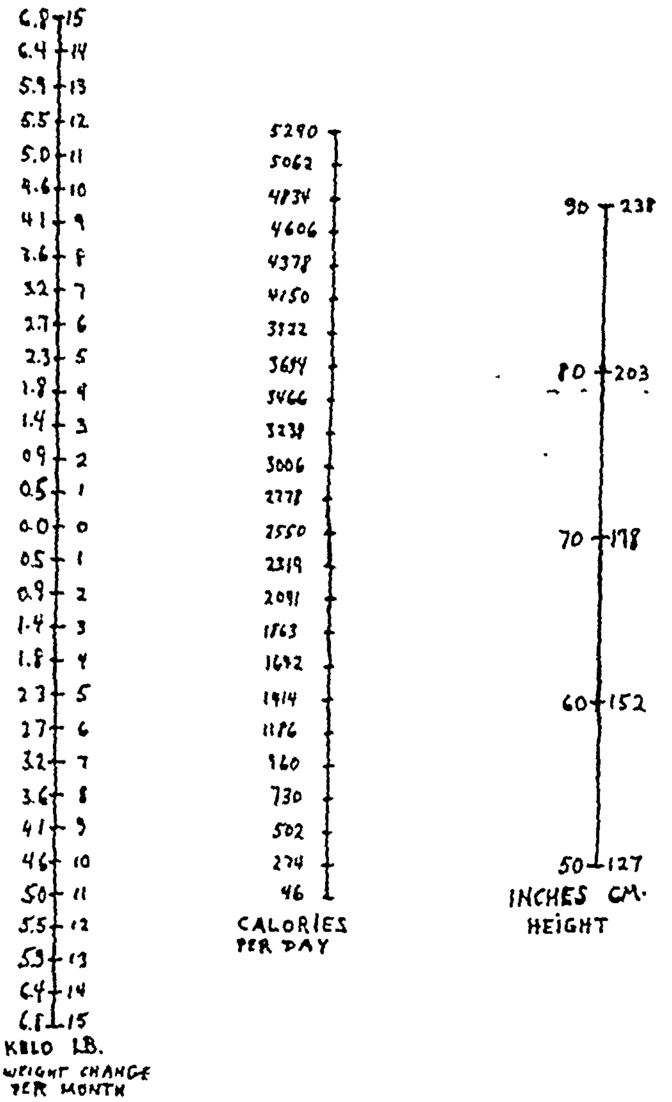
than the ideal diet per day to lose 11 lb. in one month; (4) the ideal weight is 110 lb. for the first 5 ft., plus 30 lb. for the additional 6 in. This 140 lb. is approximately 64 kg. At 35 calories per kilogram of body weight, the "ideal" diet is 35 × 64, or 2,240 calories per day; and (5) deducting the required amount (2,240 − 747) gives 1,493, or roughly 1,500 calories per day to produce the desired rate of weight reduction.



Nomogram for calculation of weight-changing diets. Select the patient's height along the right margin and the rate of weight loss or gain desired per month along the left margin. The line connecting these two points crosses the calorie line at the desired daily caloric allowance.

While this type of calculation is simple, it is rather time-consuming. The method can be reduced as follows to a general equation that will cover all cases of moderately sedentary adults. Let H = height in inches, L = pounds per month weight loss (or gain) desired, and C = calories per day. Then, the ideal weight is 5(H − 60) + 110, and the ideal diet in calories per day is

$$35\left[\frac{5(H-60)+110}{2.2}\right].$$

The pounds of fat and of water lost per day are converted to calories lost per day by the term

$$\frac{L \times 9 \times 1{,}000}{2.2 \times 2 \times 30}.$$

The difference between these two terms gives the required number of calories:

$$C = 35\left[\frac{5(H-60)+110}{2.2}\right] - \frac{L \times 9 \times 1{,}000}{2.2 \times 2 \times 30}.$$

This may be further simplified to

$$C = 11.4\,(7H - 266 - 6L).$$

Yet another saving of time and effort may be introduced by constructing a nomogram based on this general equation, by which caloric allowances may be selected at a glance for any desired weight change. Such a nomogram is shown in the figure, based on a standard requirement of 35 calories per kilogram of body weight.

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RAPID ESTIMATION OF BLOOD GLUCOSE CONCENTRATION WITH ORDINARY TES-TAPE

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An instantly available diagnostic aid and therapeutic guide for the rapid estimation of blood glucose concentration has been conspicuous by its absence. Previous attempts to meet this need by streamlining the usual time-consuming laboratory procedure have included those of Wilkerson and Heftmann [1] and Leech and Woodford,[2] as well as the use of Dextrotest, a simplified blood sugar test outfit. These attempts have not met widespread acceptance because they require special equipment that is cumbersome to operate. An indicator paper known as Tes-Tape is now being increasingly used by patients with diabetes for the detection of urinary glucose. The green-blue spectrum appearing on the yellow Tes-Tape is indicative of the presence of glucose, since the color development depends upon the oxidation of glucose by its specific enzyme, glucose oxidase.[3] The advent of Tes-Tape has enabled development of a rapid and simple means for approximating the blood glucose level. By the method to be described, within three minutes after venipuncture severe hypoglycemia or frank hyperglycemia can be distinguished from an essentially normal blood sugar level. Within another few minutes the blood glucose value can be bracketed with an accuracy varying from 25 mg. per 100 cc. at very low concentrations to 200-250 mg. per 100 cc. at high concentrations of blood sugar.

Materials and Methods

Determinations of glucose in whole blood and plasma were performed in duplicate on 130 specimens of oxalated venous blood by the "true blood sugar" method.[4] The glucose content of each sample of plasma was

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simultaneously estimated with Tes-Tape by two different techniques. The first method involved the use of undiluted plasma. One drop of plasma was placed on one end of a strip of Tes-Tape about 1.5 in. in length. Sixty seconds later the darkest color that had developed was compared with the Tes-Tape color card and read on a scale with gradings from "4+" down to "trace" or "faint trace."

The second method involved the use of serial dilutions of plasma. When hyperglycemia was anticipated or when the approximate blood sugar level was unknown, eight small test tubes (e. g., Kahn tubes) were placed in a test-tube rack. Plasma was put into an end tube, and 10 drops of distilled water were added by medicine dropper to each of the other tubes. Ten drops of plasma were mixed with the water in the second tube, and serial dilutions from 0 to 1:128 were obtained. Correspondingly fewer dilutions were made if a normal or low glucose concentration was expected. Eight strips of Tes-Tape about 1.5 in. long were then placed side-by-side on a white paper background. To one end of each strip a single drop of a successive dilution was applied. The "end-point" was that dilution of plasma showing at one minute the last definite greenish tint on the yellow Tes-Tape. The end-point was usually sharp, but comparison with a blank—a strip of Tes-Tape moistened with water—occasionally facilitated decision regarding the last positive dilution. Figure 1 shows the results of the testing by this method of two samples of plasma for which the corresponding blood sugar levels were 93 and 311 mg. per 100 cc.

Results

Blood glucose concentrations of the 130 specimens ranged from 16 to 760 mg. per 100 cc. With few exceptions their corresponding plasma glucose values were slightly higher. The absolute increase of plasma over blood sugar levels varied from -7 to 88 mg. per 100 cc. (mean of 12 mg. per 100 cc.), with the greatest increments accompanying the highest blood glucose concentrations. In all instances blood and plasma values correlated so closely that the Tes-Tape response to plasma glucose reflected the corresponding blood glucose level.

The degree of glycemia could be quickly estimated by use of either of two indexes. A very rapid approximation was provided by the Tes-Tape reaction to undiluted plasma alone. Figure 2 illustrates that, despite considerable overlapping of the color readings for a given blood sugar value, the following interpretations of clinical utility were obtainable: 1. No color or the faintest green tint (faint trace) was evidence of severe hypoglycemia. 2. A pale green of variable intensity (trace to 1+) embraced a wide spectrum extending from very low to moderately elevated blood sugar values. 3. A deep-green color alone (2+) or one merging into blue (3+) signified progressive degrees of hyperglycemia. One factor contributing to the grossness of the interpretation from undiluted plasma was the frequent difficulty in deciding between trace and 1+ or between 2+ and 3+ readings.

Precision in estimating the blood sugar concentration was sharpened considerably by determination of the end-point, as described, for serial dilutions of plasma. Figure 3 demonstrates that the dilution technique permitted much better discrimination between hypoglycemia and normoglycemia. Degrees of hyperglycemia were also distinguished more exactly when the weakest dilution to show a color change on Tes-Tape was read. Not infrequently, however, it was still impossible to differentiate normal fasting blood sugar values from moderately elevated ones. The table is derived from the graphic data shown in figure 3. At each dilution of plasma recorded as the end-point, 90% or more of the corresponding blood glucose values fell within the range indicated. The glucose content of a specimen whose Tes-Tape response ended at or before the 1:2 dilution was alarmingly low, and an end-point at 1:4 still signified clinically important hypoglycemia in most cases. On the whole, the 1:8 dilution end-point indicated either slightly subnormal or normal sugar concentrations. At the 1:16 dilution the corresponding blood sugar value was either in the normal fasting range or moderately high. Positive responses at succeeding dilutions uniformly meant proportionately elevated glucose levels.

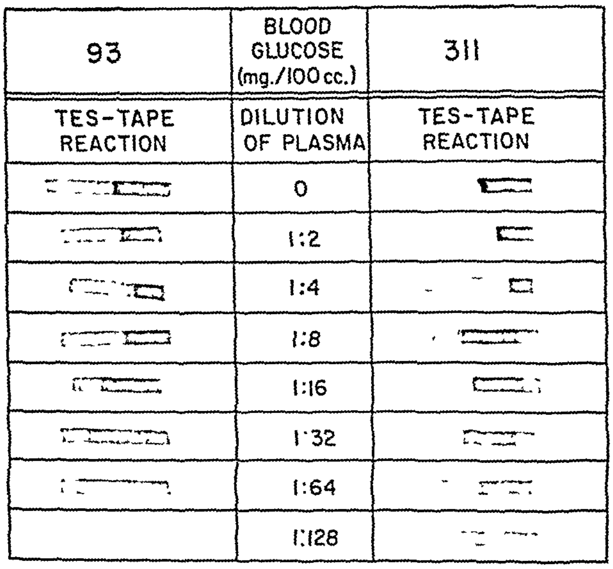

Fig. 1.—Tes-Tape indexes of two samples of plasma for which corresponding blood glucose concentrations are 93 and 311 mg per 100 cc On left, undiluted plasma shows 1+ reaction and last positive dilution is 1:16, on right, respective readings are 2+ to 3+ and 1:32. Two lower strips in each column show slight shadow cast by negative dilutions.

Comment

Depending upon the clinical information desired, the very rapid answer obtained from the Tes-Tape reaction to undiluted plasma may provide sufficient information to render a further plasma-dilution test unnecessary. For example, extreme hypoglycemia and severe hyperglycemia are instantly apparent. However, since the gradation between readings of trace and 1+ or 2+ and 3+ is often indistinct, the much closer approximation made possible by the serial-dilution technique more than compensates for the small additional investment of time.

During the development of the method, certain practical points of procedure became evident, recognition of which should facilitate duplication of the results reported: 1. Only one drop of plasma or its dilution should be placed on the Tes-Tape strip. There should be enough liquid to permit a slowly advancing fluid front during the minute of color development, but a dry area must remain at the time of reading, as shown in figure 1. If the strip is flooded, the excess of glucose-containing solution leads to overreading of the end-point by one or more dilutions. 2. The reading should be made promptly at from 60 to 75 seconds. Not only do some negative dilutions develop a greenish tint after 90 seconds but a blank of Tes-Tape moistened with water sometimes shows a similar color change after a few minutes. Apparently, the indicator in the Tes-Tape system is activated minimally and nonspecifically by water *per se*. 3. There are no false-positive readings, since the enzyme upon which color development depends reacts specifically with glucose.[3] Neither the slight hemolysis sometimes present in plasma nor coexistent high blood levels of fructose interfere with the Tes-Tape response to the glucose concentration.

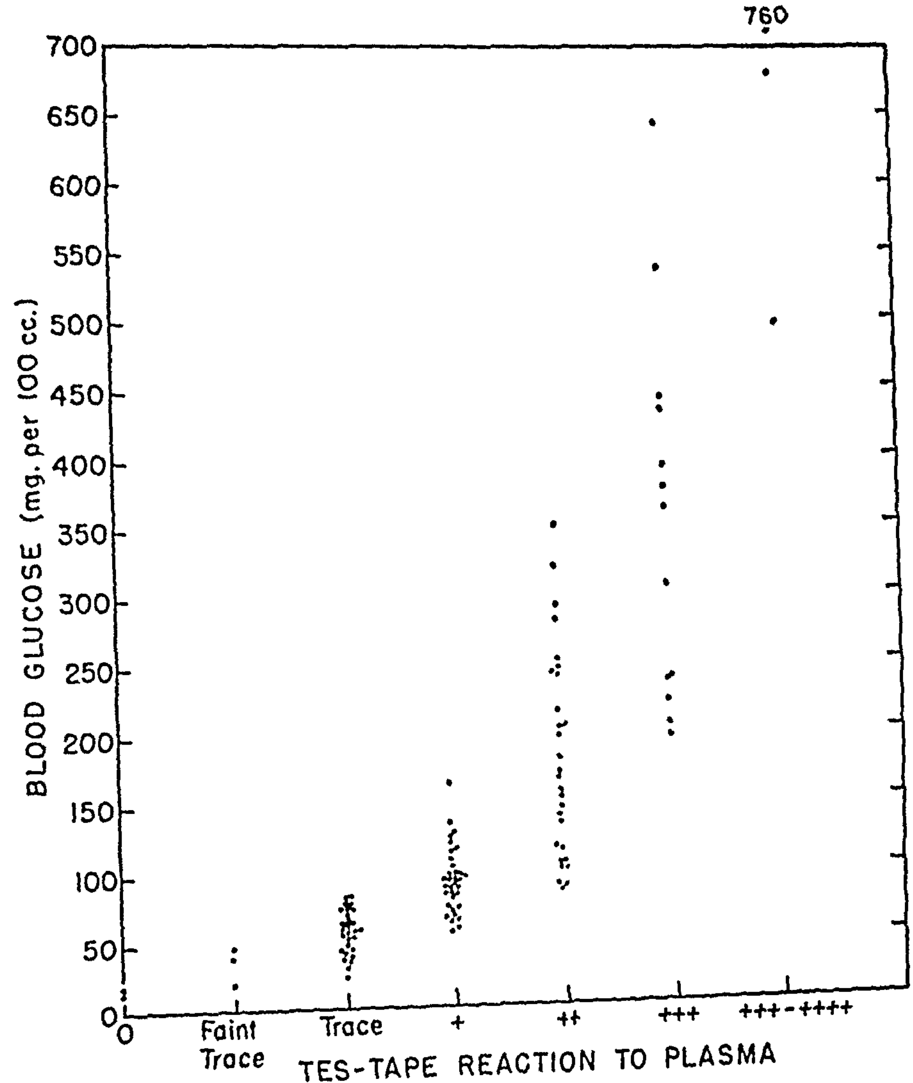

Fig. 2.—Correlation of blood glucose level with Tes-Tape reaction to undiluted plasma. Extreme hypoglycemia and frank hyperglycemia are recognizable, but grossness of reading index prevents good discrimination at intermediate sugar concentrations.

The rapidity with which this simple procedure informs the physician of the approximate blood sugar level of his patient makes it a useful adjunct in several clinical situations. In the emergency room, hypoglycemic coma can be quickly distinguished from other forms of unconsciousness. In the former case, the Tes-Tape will show at best a faint green reaction to the undiluted plasma and be negative beyond the 1:2 dilution, whereas for patients in any other state it will yield a positive response past the 1:4 dilution. On the diabetic ward of the hospital occasions frequently arise when one suspects that a patient may be hypoglycemic. Although the Tes-Tape color response is not keen enough to distinguish mild hypoglycemia from low-normal glucose values, it can easily single out a patient whose symptoms may well be due to hypoglycemia from those with obviously normal or elevated blood sugar levels. The Tes-Tape procedure can also be used conjointly with the method of Duncan and Gill[5] for estimating plasma acetone levels in order to follow the clinical course of a patient in diabetic coma. In the latter test, the diminishing intensity of color change produced by serial dilutions of plasma on the nitroprusside reagent heralds the disappearance of ketosis and a rising carbon dioxide–combining power. Similarly, a falling blood glucose level is signaled by a progressive decrease in the plasma dilution causing the last greenish tint to appear on Tes-Tape.

In addition to the above obvious applications of Tes-Tape, it may also prove useful in the screening of specimens of blood during diabetes-detection programs. The simplicity of the technique overshadows the fact that the Tes-Tape response is slightly less precise than that of the Wilkerson-Heftmann method,[1] the use of which is limited to a few diagnostic centers because of the special equipment and training required. Moreover, once plasma has been separated from red blood cells, the glucose concentration remains virtually unchanged for 48 hours or longer, so that a multitude of samples can be collected and screened en masse. On undiluted plasma, a Tes-Tape response of 3+ would automatically make the donor suspect, and a 2+ reaction would warrant further investigation if serial dilutions remained positive at 1:32 or higher.

Correlation of End-Points of Tes-Tape Response with 90% or More of Corresponding Blood Glucose Concentrations

Dilution of Plasma	Blood Glucose Values, Range of Mg./100 Cc.
0	15-20
1:2	20-40
1:4	35-65
1:8	45-95
1:16	75-165
1:32	145-355
1:64	225-450
1:128	500-760

A final word about the probable future of this test relative to its present status: It is almost certain that we shall ultimately see the development of vastly improved paper indicator systems whereby direct, instantaneous, and highly accurate assessment of the plasma glucose level will be possible. When that happens, ordinary Tes-Tape will become as obsolete as litmus paper. In the meantime, however, the comparatively gross information provided by the method described does not discredit its general applicability today. Here, for the first time, by the use of a "litmus-paper" technique and a material that is available in all pharmacies, valuable information can be quickly obtained regarding the blood sugar concentration of the patient.

Summary and Conclusions

A simple technique, based upon the color response of ordinary Tes-Tape to plasma, enables rapid gross estimation of the blood glucose concentration. Either severe hypoglycemia or frank hyperglycemia can be instantly distinguished from normal blood sugar values by observing the Tes-Tape reaction to undiluted plasma. More precise information is obtained by determining the color response to serial dilutions of plasma. This procedure offers a range of accuracy that is proportional to the actual level of glucose in the blood. At glucose concentrations that are below 50 mg. per 100 cc. one can usually read within 20 to 30 mg. per 100 cc., while at very high levels the reading range widens to 200 to 250 mg. per 100 cc. The simplicity and rapidity of the test and the availability of materials recommend the test for general use whenever prompt information regarding the patient's approximate blood sugar level is desired.

4500 S. Lancaster Rd. (2).

This study was supported in part by a grant from the U. S. Public Health Service.

The Tes-Tape used in this study was supplied by Mr. Walter H. Stein of Eli Lilly & Company, Indianapolis.

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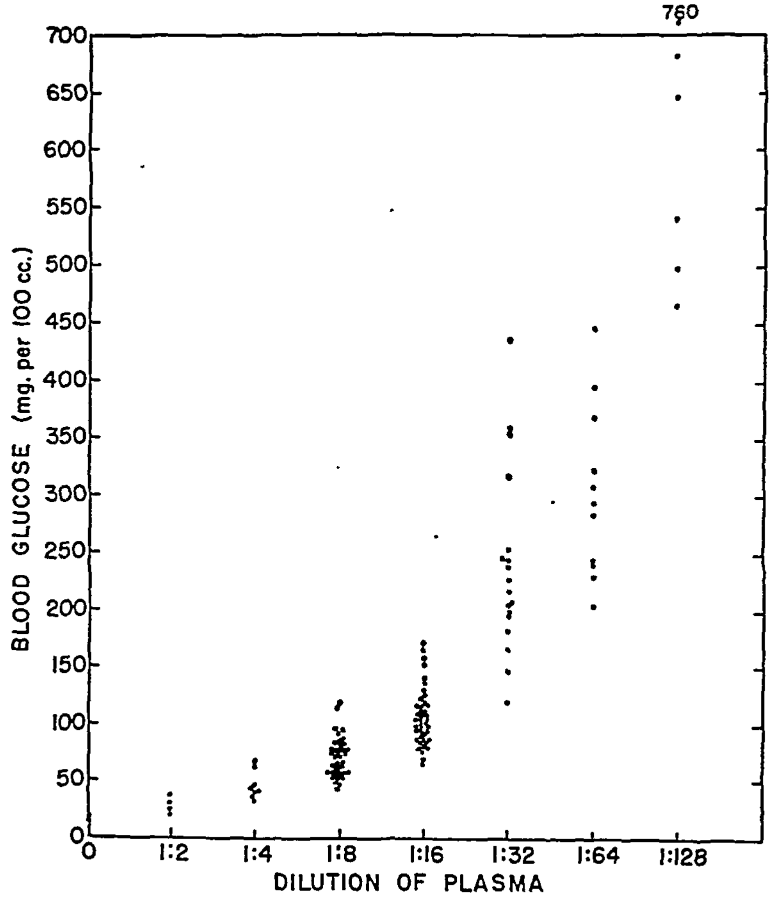

Fig. 3.—Correlation of blood glucose level with end-point Tes-Tape response to serial dilutions of plasma. Degrees of hypoglycemia and hyperglycemia are satisfactorily interpreted. Normal sugar values may or may not be distinguishable from moderately elevated ones.

MEDICINE AT WORK

THE DOCTORS WHO TALK ABOUT WAR

Around a green baize-covered U-shaped table in Washington, D. C., two dozen doctors were talking about a war they hope never will come. What they heard and said might some day affect not only physicians but all Americans in every walk of life. Here, published for the first time, are elements of that story as it was unfolded last Oct. 25 by representatives of a dozen federal agencies at the meeting of the Committee on Civil Defense, Council on National Defense, of the American Medical Association.

News Item

The U. S. Federal Civil Defense Administration revealed that the government now is completing a prototype of a plastic "basic protective mask" in six shapes and sizes for possible civilian use against chemical warfare. Dr. John M. Whitney, who is director of the health office of the FCDA, told the committee that if and when the government decides there should be mass distribution of the masks, the FCDA simply will rush sets of master molds to manufacturers across the country. The factories then can produce the masks quickly by a plastic injection method. Until now, the FCDA had considered air pollutant defense secondary to nuclear war effects.

Dr. Whitney also announced that medical supplies for three and a half million casualties over a three-week period now are stored in 40 warehouses across the United States and that by 1958 the cache will be big enough for five million victims of any national catastrophe.

News Item

The Atomic Energy Commission's long-awaited new handbook on the effects of nuclear weapons is now in final proof and will be available for distribution in a few months. Robert L. Corsbie of the AEC's division of biology and medicine says the handbook will be in less technical language than a now-outdated edition, and "will be accessible to many more non-scientific people." The publication is expected to answer, for the general public, many persistent questions about radiation and biology associated with H-bomb explosions.

It also may answer criticism that the present administration in Washington has tried to suppress disturbing reports on the dangers of radiation. Said Corsbie: "We believe now that although the law justifiably keeps nuclear devices classified (as secret), information from field tests should be made public. As a result, three-fourths of our 47 weapons test reports will be made available soon." Corsbie, who was on a Navy survey team at Hiroshima in 1945, also revealed that an important re-survey of A-bomb effects in Japan is producing some new and valuable data.

For example, a medical survey team 10 years ago "documented" the case of 100 persons who survived the blast at Hiroshima by seeking shelter in a cave. But last year another team, working with Japanese physicians, carefully reconstructed conditions at the same cave and found that the refugees actually numbered 67, of whom only 2 survived. Says Corsbie: "We feel that if we are wrong on early findings, we should say so. For example, we have thrown out a theory that blast and radiation burns occur only when the victim is in open-line sight of a nuclear blast. That theory was disproven when the explosion of a 15-kiloton device from a 300-foot tower caused burns around the eyes and groin of dogs which were 1,500 feet away in a shelter built with two right-angle turns."

News Item

A nationwide network of "revitalizing" teams is being organized by the U. S. Air Force to speedily restore combat crews into retaliatory shape in case they are hit by an enemy attack. Air Force Col. Joseph Nagle announced that by 1958 eight of these 118-man "casualty management and control" units will be set up near (but not in) Strategic Air Command base areas. He says: "If as a result of these units we can launch one more B-52, they will have paid for themselves." Civilians would not be served by these Air Force units. They would have to "shift for themselves" through their local civil defense organizations and would, in fact, be expected to give medical aid to the military (instead of vice versa) during the early stages of an enemy attack.

Other News

Other news was occurring in that hotel meeting room—news about expanded civil defense training for public health reservists, about a nationwide survey of community water systems, about a few AEC advances against radioactive fallout, and about continuing government research on the effects of nuclear explosions and of biological and chemical warfare contaminants on foods and drugs.

Dr. Harvey Stone of the health resources advisory committee of the Office of Defense Mobilization told the physicians that, to his great surprise, he learned that a single nuclear bomb could wipe out all three U. S. firms that manufacture surgical instruments. Almost the same geographical proximity is true of x-ray equipment companies in this country, he said. It was something to think about.

And there was something else to think about: In case of enemy attack, where does a physician's responsibility lie? Does he rush to duty at his hospital or does he rush into uniform from reserve status? Is

Left, civilian protective mask being developed for possible mass use against chemical warfare. The Federal Civil Defense Administration says that the mask—designed in six variations of shapes and sizes—can be produced in local factories by a plastic injection method. The FCDA would keep the master molds.

Middle, Los Angeles—American Red Cross demonstration of what an "emergency disaster" would be like. Although it was not said, this could have been a cross section of the aftermath of an A-bombing. Realism was added by administration of blood plasma to "victims."

Right, in Flint, Mich., June 11, 1953, "Tornado's Toll," injured residents of Flint lined row on row in the gymnasium of the wrecked school, after the emergency shelter was set up to meet the need of treating injured and homeless when hospitals in the area became packed with casualties. More than 125 persons were killed and many hundreds injured in the violent twister.

it his prime obligation to fulfill key duties in his state civil defense organization, or at the nearby first-aid station—or at the stricken factory where he may have been employed part-time? For many physicians, it can be a multi-responsibility beyond their priority control.

Already, the ODM has a special task force working on the problem. The A. M. A. Committee Chairman, Dr. Harold Leuth, suggested to his colleagues: "The matter of a doctor's dual responsibility is a top cabinet decision in our government." This doctors' dilemma has not yet been resolved; it still is being considered.

Members also are considering the stark contrast of civil defense in this country and in Great Britain. They heard U. S. Army Col. Joseph R. Schaeffer, recently returned from three days in England, say: "The British are very alert to disaster situations. They continually are exercising for atomic war. I saw one man who travelled 200 miles to London at his own expense—just so he could lie in the rubble of a street, as a casualty model wearing realistic-looking wounds. He was observed and worked over by students, passersby, even members of Parliament—all of whom were eager to learn what they could do to help themselves in a disaster. There is nothing like it done in this country. In the extreme apathy in the United States, many of us are geared to believe it won't happen."

Doctors Are the Pathfinders

Nothing like it in this country? A committee member, Dr. Carroll Hungate, questions that. Admittedly, many states have fallen down on civil defense, he said, but others—including California, New York, and Kansas—are pretty well prepared. Dr. Hungate cited a recent exercise in Stanley, Kan., where nonmedical people cared for simulated casualties, and evacuated their entire town to a school house 35 miles away. He said: "In many states doctors have been and are stimulating other people and agencies into civil defense activities. They were in civil defense long before others were." Said another committee member, Dr. Cortez F. Enloe Jr.:

"From the moment the first attack warning comes, something you're doing will be affected by the civil defense measures now planned. This holds true whether you are practicing pediatrics in Paducah or plastic surgery in Manhattan. . . . The ultimate success of the national civil defense program and of the programs of the American Medical Association, of the state, and of county medical societies depends, in the final analysis, not on what authorities think and plan but on what the individual physician does. . . . For the physician, civil defense is a personal matter."

It was an immediate personal matter for hundreds of northern California physicians last Christmas when they put aside holiday plans in order to implement their own long-standing civil defense plans—and thus helped reduce the toll of human life during ravaging floods. It was an immediate personal matter for hundreds more, including 42 public health reservists called to active duty, during last year's New England floods. It was an immediate personal matter for the county medical society members in Fremont, Mich., as they took up the grim task of sorting casualties from a devastating one-two punch delivered by twin tornadoes. Wherever there has been natural disaster, it was the prearranged civil defense blueprint of local medical societies that served the community. And it was during these same disasters that the societies without civil defense training saw higher casualty figures; comparative records across the country prove that.

How to instill civil defense unity without uniformity among this nation's medical men is a major objective of the A. M. A. Committee. One suggestion being considered is the formation of a "national medical board" made up of one doctor from each state medical organization, which would offer ideas for survival. These locally applicable ideas then could be transformed democratically into specific standards and training duties, extending to the county level. As a result, doctors then might be able to do more than just vaguely "help" in their community's civil defense.

Simple geometrics makes it plain that the physician's role in a community disaster is multiplied a thousandfold when a catastrophe strikes the nation. The doctors themselves clearly defined their mission last June when their A. M. A. House of Delegates overwhelmingly voted approval of a national civil defense resolution stating:

"It is therefore the solemn duty of the medical profession, including every individual physician in the country, to exercise his skills, knowledge and best judgment to prevent human suffering and loss of life and to assume responsibility for solution of the complex medical problems arising from instantaneously produced mass casualties."

Pancreatic Insufficiency.—A number of children with cystic fibrosis of the pancreas with complete pancreatic enzyme deficiency as well as a number of healthy children were studied to determine whether the response of their plasma proline levels to the feeding of either gelatin or casein could be used as a simpler and more generally useful diagnostic test. A new simple method for the determination of plasma proline has been found suitable, and its application indicates that it can be used in conjunction with or that it may replace the glycine method The proline method has the advantage that it may be applied after casein or gelatin meals, whereas the glycine method is useful only after gelatin meals. Children with cystic fibrosis of the pancreas with complete pancreatic insufficiency have a fasting proline plasma level much below that of healthy children, whereas the fasting aminoacetic acid levels are approximately the same. The administration of a proteolytic enzyme preparation, papain, with the test meal of gelatin to patients with pancreatic insufficiency results in a significant improvement in protein digestion.—B. S. Gould, Ph D., and H. Shwachman, M.D., Studies in Cystic Fibrosis, A. M. A *Journal of Diseases of Children,* June 1956.

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION
Edited Under the Direction of the Board of Trustees
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Subscription price . . . Fifteen dollars per annum in advance
Cable Address . . . . "Medic, Chicago"

TRAINING OF THE FAMILY DOCTOR

GUEST EDITORIAL

Charles S. Davidson, M.D.

"Everyone wants and should have a family doctor." "This is the age of specialization." "Generalists are our family doctors of the future." "Someday we'll have a doctor for every part of us." "You don't get the personal medical care you used to." "The internist is the general practitioner-of-today." "We must consider the patient as a whole." These statements and many others are from physicians, editors, and lay people. Their variety and very number demonstrate that something is afoot. True—and it is just this: The complexity of modern medicine demands specialists; yet each of us when ill wants a doctor who understands us and will "see us through," who will consider the social, economic, and emotional problems as well as the pain. We might like our family doctor to take care of our glioma, yet we know that a neurosurgeon can do it better. This dichotomy between family doctor and specialist runs throughout medical practice and has given rise to the clichés above as well as to much heated discussion. Part of the heat of the discussion arises from lack of proper definition of a few words.

Let us use the term family doctor for one whom we call first when we are ill, to whom we go for "health examinations"—a physician who knows us as thoroughly as anyone can. Now who is best trained to do this, to be our family physician? Some say the generalist (general practitioner), who is (theoretically) qualified to some extent in all aspects of medicine; some say the internist; and some hope that every physician (including the neurosurgeon above) is capable of such complete medical care.

When we choose a family doctor we want to know not only about his intellectual and moral qualifications but also about his training and experience. Assume that a young man is about to graduate from medical school and wants to be a family doctor. Assume also that he has a fine mind, is morally sound, likes people, and will "make a fine doctor." What advice should he be given for his further training? He does not wish to specialize in surgery, obstetrics, neurology, or psychiatry but wants to be a good doctor. My thesis and my advice to the young man follows. No one can do major surgery, specialized surgery, obstetrics, gynecology, and psychiatry without extensive training in each subject. A person who may do all or most of these and do them well should have, after internship, intensive training and experience for at least four or five years after medical school. He is then qualified to start general practice as defined above. One year of rotating internship today is not enough to permit him to undertake all these things and do them well. In fact, general practice, as I see it, requires more years of intensive training than do many specialties. That this is beginning to be recognized is implied by the formation of general practice residencies by some hospitals. Whether many persons can afford the years of training necessary to become well-trained generalists may be doubted.

If our young man does not want to or is not able to spend this time but still does not want to be a specialist, what is he to do? I would recommend that he spend two or perhaps three years in hard hospital work, much of it in general medicine. During this time he will have worked with specialists such as surgeons, pediatricians, obstetricians, and psychiatrists and will have learned much about the problems with which they are dealing. He will thus be trained to be a family physician—not to do major surgery and probably not obstetrics, unless necessary in his community (and then he will take training), and perhaps will need to refer some or all children's problems to his colleagues in pediatrics. But he is trained to care for everyday problems and illnesses in the family. Perhaps he may wish to specialize in internal medicine, even in one of its subspecialities, and may become qualified for admission to and be certified by the American Board of Internal Medicine, but this is by no means necessary nor usually advisable for his training as a family doctor. Parenthetically, many internists are family physicians today. As the physician grows older and becomes more widely experienced, consultation practice may fall his lot. Just as likely, and in spite of experience and even "boards," he may be happier and be of greater service continuing as a family doctor, calling on others with specialized training when necessary.

Whatever the course of his professional career, our young man will be sufficiently well trained never to undertake that for which he is not qualified. In this "age of specialization," the practice of medicine will continue in its best tradition if each physician does only that which he is capable of doing well, irrespective of postgraduate diplomas and recognition by specialty boards and other approving authorities, for these latter are only gross "paper" standards. A physician's knowledge of his capabilities and his own conscience are far better standards for his conduct as a physician and as to the kind of practice he will undertake than the titles others may give him on the basis of credentials, examinations, and years of residency training. To illustrate: If our young man, after four years of medical school and one of rotating internship, assays to practice medicine, sur-

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From Thorndike Memorial Laboratory, Boston City Hospital.

gery, and obstetrics, he is fooling not only himself but his patients. So also is the expert neurosurgeon who, unaided, treats diabetes, hypertension, and the occasional obstetric case.

Let us then redefine the kinds of physicians in modern terms and say that the general practitioner will need sufficient training (four or more years after medical school) to permit him to practice medicine, surgery, obstetrics, and other specialties. The family doctor who "knows us best" and "sees us through" as far as his training and capabilities will allow may be such a general practitioner, or, more likely, he will have had far less training—the majority of it in medicine. The specialist has the kind of mind and the training to dig deep into a particular field—be it orthopedic surgery, psychiatry, or cardiology—and probably will have neither the time nor the inclination to be a family doctor, although this does not imply that he is any less a physician in the best sense of the word. We must do well that for which we are trained, but only that of which we are capable.

MEDICINE AND THE ARMED FORCES

Physicians about to perform their military obligation for the first time, their colleagues now in service, and those who have already served would have felt quite encouraged had they witnessed the recent meeting of the Committee on Military Medical Affairs of the American Medical Association. This group, which is a part of the A. M. A.'s Council on National Defense, meets at least twice a year with the expressed hope of securing the optimal interests of the medical and allied professions to serve the nation, compatible with national defense needs. By invitation, this particular committee assists the armed forces in matters of planning for medical care, physician recruitment, reserve programs, military medical supplies, deferment policies, and many other fields where medicine and the military have a joint interest. In addition, this A. M. A. activity carefully investigates complaints, as well as accolades, from physicians who, because of present or past military duties, have written and elaborated on what appear to be either professional injustices or excellent examples of military medicine in action.

The most recent meeting of the Committee was held in Washington, D. C., this past October. Representatives (in most cases the surgeon general, along with members of his staff) of all the armed forces, the Public Health Service, the Selective Service System, and the office of the Secretary of Defense volunteered their time to discuss with the Committee items that would involve a physician and his relation to military medicine. A few of these subjects might serve to illustrate the Committee's activities.

Prime interest was of course centered around the "doctor-draft." Recent newspaper publicity has intimated that the Defense Department is not planning to ask for a continuation of this legislation. The A. M. A. representatives were interested in any future plans for the possible call-up of practicing physicians. Government spokesmen agreed on the diminishing justification of their previous viewpoints concerning this special registration and went on to explain their present concepts for maintaining an adequate number of physicians to care for military personnel. First, they plan to ask amendment of the present regular selective service act to place physicians in the same category as all other specialists occasionally needed to provide optimum security for national defense. Second, initial reports on the Career Incentive Program for Medical Officers (Public Law 497, 84th Congress) seem to indicate an increasing interest in a military medical career, with greater numbers of applications for commissions being submitted and, at the same time, fewer resignations of medical officers. In projecting their needs after June, 1957, based on the continuance of the *status quo* or on improvement in world affairs, the military felt that, by its use of physicians who would have come under the regular draft but who had been deferred to complete their education, in addition to increasing numbers of volunteers, there would be adequate and competent medical care for members of the armed forces.

Military reserve activities were fully explained to the Committee by all the services represented. New programs for reservists, with special emphasis on the potential benefits to the physician becoming a member of a reserve component in his home area, were graphically demonstrated. The Committee requested that all new reserve information be compiled in an easily readable form and published for the information of the profession.

Discussion was also held concerning the dual, or in some cases triple, responsibility of the medical reservist. Specifically, there is the situation of the reserve officer presently in government employ, as in a Veterans Administration hospital. In the event of a state of emergency, which organization has prime call on the man? In a situation where a physician or nurse is a member of a reserve component and holds a key position of supervision in a medical or teaching center, does he or she owe first allegiance to the branch of the armed forces, the affiliated institution, or to community civil defense? The A. M. A. representatives felt this was an urgent problem worthy of further detailed study and secured the assurance of the military medical chiefs not only that such investigation of the government employee–reservist was now in progress but that consideration of the priority of the nongovernment reservist would also be undertaken.

Another of the many matters explored pertained to the new Central Medical Material Supply Program. The responsibility for this particular program is now vested in the Department of the Navy for all three military services. There was an informative exchange of information and ideas, based on past war and peacetime experiences along with projected possibilities, the central theme developed being to provide the most efficient supply service when and where needed, while still maintaining the desired economy of operations.

The cooperative attitude of the military officials in working with the members of the Committee on Military Medical Affairs reflected a sincere desire to work hand-in-hand with organized medicine to achieve that evidently not impossible goal of matching military medicine to its civilian counterpart. Both groups at the meeting, each having its own responsibility—the military to the country's defense and the A. M. A. to the health and welfare of the country as a whole—obviously tried to meet each other halfway. That the meeting brought forth worthwhile discussions on the majority of topics shows this liaison between the practicing physician (regardless of whether he is an A. M. A. member) and the Department of Defense to be an effective link for improving military medicine.

RURAL HEALTH

While illness in a patient may not be clinically different whether he lives in a rural or urban community, the factors concerning the prevention and treatment of his illness vary greatly when the patient is distant from the contributions of a city medical center. Conditions leading to good health in village and country living are admittedly different from those in the more urban parts of the United States. After consideration of the recent reports on air pollution along with crowded living conditions, which are epidemic potentials, it is not impossible to envy the rural citizen. On the other hand, the farmer or rancher usually must be his own public health department, while the city resident has many preventive health measures performed for him through such environmental controls as sewage disposal and through his safe and adequate water supply. Because the rural population has demonstrated its desire to utilize available preventive techniques and, even more so, to understand better how to make the best use of professionally qualified medical care when it is available, and in view of the fact there is insufficient distribution of competent health personnel and facilities in many of these isolated areas, the Council on Rural Health of the American Medical Association has been assisting receptive communities in solving their unique health problems.

The natural problems and influences of an isolated area are not limited to environmental sanitation and animal diseases related to man but also include special adjustments to climate, nutrition, and safety. Whether it be a farm or mining community, to use just two examples, the desire for proper health education seems to be the element making these particular locations warrant special medical study. Until people become aware of a scientific total medical care program, they may be susceptible to any unreliable and unscientific advice that offers relief of aches and pains. They are equally subject to the propaganda of organizations that capitalize on remoteness and keep from them those advances in health and sanitation that would benefit their mode of living.

Rural health is not a misnomer. It is an all-inclusive term describing the path to a more healthful way of life to the citizen in the country. It is basically a lay-sponsored movement to help independent communities help themselves to healthier living by obtaining the active participation of all concerned. First, there are the programs emphasizing the preventive aspects of health, including sanitation of the environment, carried out in cooperation with public health workers. This is the groundwork that stresses the idea of personal protection from future illness and at the same time prepares the population for the acceptance of proper medical care when it is offered. Second, there is the actual providing of medical care by the recruitment of physicians, dentists, nurses, and other ancillary health personnel. These persons, despite their missionary spirit, must feel that they are really wanted and that use will be made of their skills. An example of the success of a rural health program appears in the report of Overholt and the Tennessee Medical Foundation.[1] In this instance, existing cultural patterns of misunderstanding were overcome by providing quality medical care and by having this betterment introduced by, shared with, and then earnestly desired by those who were to benefit from this progress.

While the physician should not claim a privileged position in the rural health movement, he should be available to serve in these ventures and to aid those seeking professional assistance. To solve most, if not all, of the health problems of any rural community in a manner satisfactory to the largest number of its people, the medical profession in addition to its cooperative effort must at the same time insist on self-help, voluntarily contributed.

MEDICINE DISCUSSES WAR

With tension rising and spreading in Eastern Europe and the Middle East, the sadly neglected concept "civil defense" cannot be pushed aside in the United States. Again, the nation's physicians are in the forefront of a continuing civil defense effort, keeping pace with new developments in nuclear, biological, and chemical warfare in order that they may better serve their community and nation in case of attack.

The degree to which civil defense also is a personal matter to physicians is shown repeatedly in each year's hurricanes, floods, fires, and tornadoes—natural disasters wherein the death toll is sharply reduced only when local medical societies act on their civil defense blueprints.

Latest developments to adjust those blueprints are revealed elsewhere in this issue (page 1237) from Washington, D. C., in "The Doctors Who Talk About War." It is a report of last month's meeting of federal representatives with the Civil Defense Committee of the A. M. A. Council on National Defense.

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[1] Overholt, B. M.: Role of Organized Medicine in Development of Rural Health Plans, Am. J. Pub. Health 46: 994-997 (Aug.) 1956.

THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

Like many of you, I recently received a four-page brochure urging the compulsory coverage of physicians under the Old-Age and Survivors Insurance provisions of the Social Security Act. This brochure, which gives the subject a quick and easy, "once over lightly" treatment based on questionable facts and figures, is from the committee on social security for doctors of the Physicians Forum.

The source of this material should immediately cast doubt on the accuracy and objectivity of its message. Most physicians will recall that the Physicians Forum was the only medical organization in the country that supported national compulsory health insurance and will not look kindly on any cause that it supports. Nevertheless, this is an issue on which there is room for honest differences of opinion based on facts rather than propaganda. The stepped-up activity of the Physicians Forum should stimulate all members of the profession to learn the facts about compulsory social security coverage for physicians. The issue undoubtedly will be coming up again in the immediate future.

One thing I think we should keep in mind, in order to maintain the proper perspective, is the difference between this problem and an issue like the disability benefits enacted by Congress earlier this year in H. R. 7225. The latter, and similar expansions that surely will be proposed in the future, bring the Social Security Administration closer to regulation of medical care and will have a dangerous effect on the future shape of medical practice.

On the other hand, the inclusion or exclusion of physicians under OASI, while it is vitally important to us as individuals, cannot in itself stimulate further government intrusion in the field of medical care. The issue is primarily one of personal philosophy, economics, and preferred alternatives.

On this issue, the House of Delegates of the American Medical Association has stated its opposition to compulsory coverage of physicians under OASI, although it has made it clear that there is no opposition to voluntary coverage. On the basis of all available evidence, this policy is in accord with the opinion of the majority of American physicians. For example, the House of Delegates, at the 1955 Boston Clinical Meeting, recommended that state societies poll their memberships on this question. The results, as reported at the 1956 Chicago Annual Meeting, showed that 34 state and two territorial societies opposed compulsory coverage. Only three polls could be interpreted as favoring compulsory coverage, and two of those were inconclusive.

More recently, *Medical Economics* magazine reported in its September, 1956, issue on a nationwide survey of more than 10,000 self-employed physicians. This poll eliminated the possibility of voluntary coverage and offered a choice between compulsory coverage and no coverage. The result: 59.8% favored no coverage and 40.2% favored compulsory coverage. In my opinion, the percentage in favor of no coverage will become even greater if every self-employed physician will study this issue and acquaint himself with the black-and-white realities of costs, benefits, and future probabilities.

The majority of self-employed physicians do not retire. About six out of seven doctors now in the 65-75 age group are still in private practice. It is unjust and unreasonable to force physicians to pay taxes into a system from which most of them will get little or no retirement benefits. It is well to remember also that under social security either you collect retirement benefits or your family collects survivors' benefits. It cannot be both. It has to be one or the other. But you as a self-employed physician are not likely ever to see the retirement checks. And the facts show that you can get much better, sounder, and cheaper protection for your family through private insurance companies than you can through social security taxes. This is especially true for younger physicians.

As one last suggestion, I urge you to read and reread the two articles on this subject by Drs. Webster and Coffey that appeared in the Sept. 15 and 22, 1956, issues of The Journal. There you will find an exhaustive collection of facts, figures, and examples that will help you make a decision based on knowledge rather than propaganda. Your decision and that of your professional colleagues—made known in your county and state medical societies—will determine the future policy of your House of Delegates in the American Medical Association.

Dwight H. Murray, M.D., Napa, Calif.

MEDICAL NEWS

CALIFORNIA

Hospital News.—Construction has started on a $500,000 addition to the department of diagnostic radiology at Cedars of Lebanon Hospital, Los Angeles. The expanded facilities will enable the hospital to increase its x-ray service. A conveyor system from the x-ray rooms to the darkrooms for development and to the doctors' rooms for viewing and consultation will expedite the service.

Fatal Case of Plague Reported.—According to the state department of public health, California's first known case of bubonic plague in man since 1917 resulted in the death June 25 of a 43-year-old retired Navy chief petty officer, nine days after his apparent exposure to infected fleas while he was on an outing in Lockwood Valley and Sespe Gorge areas of Ventura County. An investigation by local and state health departments disclosed a number of mummified squirrels and rabbits in the area where the man had walked from his car to do target shooting at a deserted farm. Tests by the state department of public health laboratory confirmed the case as plague resulting from a virulent strain of Pasteurella pestis.

CONNECTICUT

Phi Delta Epsilon Lecture.—The Alpha Rho chapter of the Phi Delta Epsilon fraternity at Yale University School of Medicine, New Haven, will hold its 11th annual lectureship in Yale Medical Center, Nov. 28. The guest speaker, Dr. Gustave J. Dammin, chief pathologist, Peter Bent Brigham Hospital, Boston, will discuss "Current Studies on the Survival of Skin Homografts."

Annual Clinical Congress.—The 31st Connecticut Clinical Congress of the Connecticut State Medical Society and the Yale University School of Medicine, New Haven, will convene at the Hotel Statler, Hartford, Dec. 5-6. Dr. Dwight H. Murray, Napa, Calif., President of the American Medical Association, will deliver the dinner address Thursday, 7 p. m. Registration admitting to all sessions will be $5. Medical students, interns, and residents will be the guests of the congress, if properly certified. In the ballroom Wednesday morning, "Coronary Artery Disease—Physiologic Concepts—Surgical Operation" will be presented by Dr. Claude S. Beck, Cleveland, and "Treatment of Carcinoma of the Cervix" by Dr. Howard C. Taylor Jr., New York. Simultaneously in the Boston room "Modern Treatment of Leukemias and Lymphomas" will be the topic of Dr. William Dameshek, Boston, and "Streptococcal Infections—Their Management and the Prevention of Complications" that of Dr. Benedict F. Massell, Boston. Luncheon in the ballroom will be preceded by a clinicopathological conference conducted by Dr. Joseph E. Flynn, Columbia, Mo., with Dr. Dameshek as discussant, and will be followed by a panel on the management of myocardial infarction, with Drs. Charles K. Friedberg and Irving S. Wright, New York, as collaborators and Dr. Beck as discussant. At 3:15 p. m. the Hezekiah Beardsley Pediatric Society will present "Bilirubin: A Toxic Substance" by Dr. Richard L. Day, Brooklyn, in the ballroom; "The Therapeutic Team in Child Psychiatry" by Dr. I. Peter Glauber, New York, a program arranged by the Connecticut Society for Psychiatry and Neurology will be offered in the Boston-Buffalo rooms; and "Radio-Active Fall Out" will be discussed by Gordon M. Dunning, Washington, D. C., in the New York-Washington rooms. The Thursday morning program will include "An Evaluation of the New Oral Sulfonyl-Urea Drugs in Diabetes Mellitus" by Dr. Max Miller, Cleveland, and "Treatment of Nausea" by Dr. Stewart G. Wolf Jr., Oklahoma City (ballroom), and "Diagnosis of the Acute Abdomen in Children" by Dr. Orvar Swenson, Boston, and "Management of Urinary Tract Infections" by J. Hartwell Harrison, Boston (Boston room). Luncheon in the ballroom will be preceded by a clinicopathological conference conducted by Dr. Harry M. Zimmerman, New York, with Dr. Miller as discussant, and will be followed by a panel on "Gastric Ulcer: Medical Versus Surgical Management," on which Drs. Chester M. Jones and Francis D. Moore, Boston, will serve as participants and Dr. Wolf as discussant. The scientific sessions will end with "Medical Care Plan for Dependents of Military Personnel" (speaker to be announced).

DELAWARE

Research at State Hospital.—A research division that will function as an independent unit at the Delaware State Hospital, Farnhurst, was recently initiated. Dr. Fritz A. Freyhan, clinical director of the hospital, has been appointed director of research. The following projects have been approved: (1) a clinical-sociological study of schizophrenia in Delaware; (2) clinical investigations of the effectiveness of neuroleptic drugs; (3) the effectiveness of intensive psychotherapy in patients with chronic schizophrenic psychoses; and (4) cerebral blood flow and metabolism in psychiatric disorders (for which the National Institute of Mental Health has awarded a grant of $23,500 for a five-year period). The other projects will be financed from a special research fund appropriated by the state legislature.

FLORIDA

Geriatric Seminar at Sarasota.—The Sarasota and Manatee county medical societies and the Manasota Medical Foundation will present a Geriatric Seminar, Dec. 3-7, at the Orange Blossom Hotel, Sarasota. The seminar is approved for credit for postgraduate study by the American Board of General Practice. Drs. Hal M. Davison, Harold P. McDonald, Alva H. Letton, and T. Sterling Claiborne, Atlanta, Ga., will discuss a wide range of topics, including allergy in the aged, gallbladder disease, cardiac irregularities, coronary arteriosclerosis and thrombosis, cancer of the thyroid, teaching of psychosomatics, gastrointestinal and genitourinary disturbances, prostatic obstruction, and nutrition. There is no registration fee.

ILLINOIS

Pathologists Meet in Springfield.—The Illinois Society of Pathologists will hold its fall meeting Dec. 1 at St. Johns Hospital in Springfield, under the presidency of Dr. Dennis B. Dorsey, Danville. A slide seminar, 9 a. m., will have as moderator Dr. Grant C. Johnson, Springfield, and as panel members Drs. Harold D. Palmer, Springfield, and Paul E. Steiner and Mark C. Wheelock, Chicago. A luncheon and business meeting are scheduled for 1 p. m.

Clinics for Crippled Children.—The University of Illinois division of services for crippled children has scheduled the following clinics to which any private physician may refer children for consultative services:

Nov. 27, Effingham (rheumatic fever), St. Anthony's Emergency Hospital, Peoria, Children's Hospital.
Nov. 28, Aurora, Copley Memorial Hospital, Springfield (cerebral palsy), Memorial Hospital.
Nov. 29, Decatur, Decatur and Macon County Hospital.
Nov. 30, Chicago Heights (cardiac), St James Hospital.

Chicago

Lecture on Cardiac Lesions.—The South Chicago branch of the Chicago Medical Society in cooperation with the Chicago Heart Association will present "Recognition of Common Cardiac Lesions" by Dr. Peter J. Talso, associate professor of medicine and assistant chairman, department of medicine, Stritch School of Medicine of Loyola University, Nov. 27 at 9 p. m. Audience participation and a social hour will follow the lecture, which will be delivered at the Illinois Central Hospital (cafeteria), 5800 Stony Island Ave. (phone: MIdway 3-9200).

Kaplan Lecture in Neuropsychiatry.—The Phi Delta Epsilon Foundation of Chicago announces that the 1956 Dr. Leo A. Kaplan Second Annual Lecture in Neuropsychiatry, "Influence of Psychosomatic Concepts on General Medicine," will be delivered by Dr. Theodore Lidz, professor of psychiatry, Yale University

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

School of Medicine, and psychiatrist-in-chief, Yale Psychiatric Institute, New Haven, Conn. Dr. Lidz, who is president-elect of the American Psychosomatic Society, will speak at the Drake Hotel, Nov. 29, 8 p. m. All physicians and interested persons are invited.

MASSACHUSETTS

Personal.—Dr. John M. Kinney, senior assistant resident surgeon, Peter Bent Brigham Hospital, Boston, has received the second annual Mead Johnson Award for Graduate Training in Surgery. The award, made through the scholarships committee of the American College of Surgeons, provides $3,000 annually for a three-year period. Dr. Kinney's studies are concerned with methods that could be utilized postoperatively either to increase the level of conversion of carbohydrates into energy or to provide increased amounts of carbohydrates for the metabolic process.

MICHIGAN

Dr. Karsner to Give Weller Lecture.—The Michigan Pathological Society has announced the establishment of the Carl V. Weller Lectureship in recognition of the contributions made by Dr. Weller in the fields of pathology and clinical pathology. The first lecture will be given in Ann Arbor, Dec. 8, by Dr. Howard T. Karsner, Washington, D. C., medical advisor to the Navy.

Personal.—Donald G. Marquis, Ph.D., chairman, department of psychology, University of Michigan, Ann Arbor, has been appointed a member of the National Advisory Mental Health Council, the surgeon general, U. S. Public Health Service, has announced. This council advises and makes recommendations to the surgeon general regarding activities of the National Institute of Mental Health.

MINNESOTA

Personal.—Dr. Edward A. Meyerding, St. Paul, executive secretary, Minnesota Tuberculosis and Health Association, has been awarded the William G. Anderson service award by the American Association for Health, Physical Education, and Recreation for his work in developing better health programs and environment for Minnesota school children. Dr. Meyerding's public health career began in 1909 with his appointment as director of hygiene of the St. Paul public schools.

NEW JERSEY

Society News.—The New Jersey Orthopedic Society recently elected Dr. Bernard M. Halbstein, Long Branch, president; Dr. Harold T. Hansen, South Orange, president-elect; Dr. Otto Lehmann, Long Branch, secretary, and Dr. John M. Naame, Atlantic City, treasurer.

NEW YORK

Meeting on Industrial Medicine.—The New York State Society of Industrial Medicine, will hold its annual meeting at the Hotel Roosevelt, New York City, Dec. 6, 4:30 p. m. "Radioactivity and Its Applications, with Particular Reference to Industry" will be discussed by Samuel A. Lough, Ph.D., deputy director, health and safety laboratory, Atomic Energy Commission; "Radioactive Fall-Out" by John H. Harley, Ph.D., chief, analytical branch, health and safety laboratory, AEC; and "Biologic Effects of Radiation" by Henry A. Blair, Ph.D., director, atomic energy project, University of Rochester School of Medicine and Dentistry. Cocktails and dinner are scheduled for 7 p. m. Requests for reservations should be sent to Dr. Harry E. Tebrock, New York State Society of Industrial Medicine, 1740 Broadway, 14th Floor, New York 19.

New York City

Conference on Mental Hygiene.—All directors of clinical laboratories and senior pathologists of the New York State Department of Mental Hygiene have been invited to participate in a one-day conference at the New York State Psychiatric Institute, Nov. 30, 9 a. m.-5 p. m. The program will feature a neuropathological seminar on diagnostic problems and unusual neuropathological conditions; a symposium on liver pathology in relation to recently used pharmacological therapy in mental disorders; and a series of scientific papers on clinical-pathological reports.

NORTH CAROLINA

Annual Gaston Symposium.—Dr. Nicholson J. Eastman, professor of obstetrics and director of the department of obstetrics at Johns Hopkins University School of Medicine and obstetrician-in-chief at Johns Hopkins Hospital, Baltimore, will be the guest speaker for the fifth annual Gaston Memorial Hospital Symposium in Gastonia, Nov. 28. Dr. Eastman will speak at 4 p. m. on "Apnea Neonatorum." His topic for the evening meeting will be "Maternity Care in Global Perspective." All sessions will be held at the Masonic Temple.

OHIO

Grant for Leukemia Study.—The John A. Hartford Foundation has made a grant of $162,075 to the Toledo Hospital for a three-year study of the causes and treatment of leukemia. The study will be conducted under the direction of Dr. Bernhard Steinberg, director, Toledo Hospital Institute of Medical Research, in conjunction with a group consisting in part of a clinical hematologist, Dr. Muvaffak A. Atamer, and a biochemist, Leon Libenson, Ph.D. The investigation is a transference of the basic research done at the institute for the past 11 years.

Seminar on Obstetrics and Gynecology.—The Southwestern Ohio Society of General Physicians in collaboration with the Cincinnati Obstetrical and Gynecological Society and the University of Cincinnati College of Medicine, offers a seminar on obstetric and gynecologic problems Nov. 26, in the medical school auditorium (emergency call answering service, AVon 1-2568). Among the topics to be discussed are bleeding in early and late pregnancy and after delivery; management of prolapse of cord and of convulsions; amniotic fluid embolism; aspiration during anesthesia; abnormal vaginal bleeding before menopause and postmenopausal bleeding; and pelvic pain. A question-and-answer period is scheduled for 3:15 p. m.

OREGON

Society News.—Dr. Herman A. Dickel, Portland, president-elect of the Multnomah County Medical Society, was recently elected charter president of the Portland Psychiatrists in Private Practice, an organization designed to study the situations, information, and problems incidental to the private practice of psychiatry. Other charter officers are Drs. Siegfried R. Berthelsdorf, Portland, secretary-treasurer, and DeWitt C. Burkes, Portland, executive committee member.

Course on Allergy.—A postgraduate course on allergy will be given Dec. 3-5 in the auditorium of the University of Oregon Medical School, Portland, under the sponsorship of the division of allergy of the medical school, the Allergy Society of Oregon, and the American Foundation for Allergic Diseases. Guest lecturers will be Dr. Ethan A. Brown, assistant professor of pediatrics, Tufts College Medical School, Boston, president of the American College of Allergists, and editor of the *Annals of Allergy*, and Dr. Orval R. Withers, associate clinical professor of medicine. The program will include round-table discussions and clinical demonstrations. Enrollment is unlimited, with a tuition fee of $25 for the course. Eighteen hours of Category I credit will be allowed by the American Academy of General Practice.

PENNSYLVANIA

Philadelphia

Ex Residents' Dinner.—The annual dinner of the Philadelphia General Hospital Ex Residents' Association will be held at the Penn-Sherwood Hotel, Dec. 4, 7 p. m.

Dr. Parkinson Accepts Reappointment.—On the request of President Robert L. Johnson, LL.D., and the executive committee of Temple University, Dr. William N. Parkinson has agreed to forego retirement plans as dean of the medical school and vice-president of the medical center and to accept reappointment in this dual capacity for an additional three-year period. The request on the part of university officials was prompted in part by the current extensive 12 million dollar expansion program at the medical center. Dr. Parkinson, who came to the medical school as associate dean in 1926, has been dean since 1929.

TENNESSEE

Personal.—John P. Quigley, Ph.D., Memphis, has been appointed by the surgeon general to serve as a member of the selection committee for the senior research fellowships granted by the National Institutes of Health.

Convulsive Seizure Clinic.—The University of Tennessee College of Medicine, Memphis, has opened a Children's Convulsive Seizure Clinic in the Pediatric Clinic of the John Gaston Hospital under the direction of Dr. James G. Hughes, professor of pediatrics. The new clinic, limited to patients of the hospital's outpatient department, will provide comprehensive diagnosis and treatment for children with convulsive seizures and undertake intensive study of the affected children.

TEXAS

New Regulations on Radiation Exposure.—The Texas State Board of Health has adopted new regulations on radiation exposure, which became effective Sept. 1. The state health commissioner, Dr. Henry A. Holle, Austin, states that these regulations are consistent with the National Committee on Radiation Protection report, which was prepared on request from representatives of the American College of Radiology, the American Medical Association, and the U. S. Public Health Service. The following points summarize the principal aspects of these regulations: 1. It requires registration of all radioactive materials and radiation-producing machines, such as x-ray equipment, within 30 days of commencement of use. 2. It establishes certain definitions, terminology, and official radiation symbols. 3. It establishes standards for air, water, and other environment. 4. It requires designation of a responsible person to be in charge of radiological safety programs. 5. It requires personnel monitoring and maintenance of records and reports under certain specified conditions. 6. It requires labeling of hazardous material and identification of areas where radioactive material is stored. 7. It requires permission prior to dumping or burying of radioactive wastes. 8. It requires reporting of accidental release of radioactive material that leaves premises of the user. 9. It requires reporting of accidental exposures received by a person when dose exceeds five times the permissible amount. 10. It allows certain specified exemptions. These regulations do not apply to the kind or amount of radiation that may be applied to a person for diagnostic or therapeutic purposes by or under the direction of a physician or dentist.

WASHINGTON

State Medical Election.—Officers of the Washington State Medical Association include Dr. James H. Berge, Seattle, president; Dr. Milo T. Harris, Spokane, president-elect; Dr. Walter C. Moren, Bellingham, vice-president; Dr. Frederick A. Tucker, Seattle, secretary-treasurer; and Mr. Ralph W. Neill, Seattle, executive secretary.

WEST VIRGINIA

Society News.—Dr. Clark K. Sleeth, Morgantown, was recently installed as president of the West Virginia Heart Association; Dr. Lynwood D. Zinn, Clarksburg, was named vice-president; Dr. James H. Walker, Charleston, secretary; and Mr. R. E. Plott, Charleston, treasurer (reelected).

Panhandle Medical Jubilee.—The Eastern Panhandle Medical Society will celebrate its golden anniversary at a banquet at the Shenandoah Hotel in Martinsburg, Dec. 1. The speaker, Dr. Louis A. M. Krause, is professor of clinical medicine at the University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, and a teacher of the history of medicine. A social hour will precede the banquet, and at the conclusion of the program there will be a reception and dancing.

Institute on Medical Practice.—An all-day postgraduate institute, regional meeting, sponsored by the West Virginia chapter of the American Academy of General Practice and the Eastern Panhandle Medical Society, will be held at the Shenandoah Hotel in Martinsburg, Dec. 2. The lecturers have been voted best in their respective categories, or as best all-around lecturers, by the seniors in the medical schools represented on the program:

Diagnosis and Treatment of Sciatica, Dr. Bernard J. Alpers, professor of neurology, Jefferson Medical College of Philadelphia.

Poisoning in Children, Dr. John E. Bradley, professor of pediatrics, University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore.

Subject to be supplied, Dr. Robert J. O. Coffey, professor of surgery, Georgetown University School of Medicine, Washington, D. C.

Subject to be supplied, Dr. Eleanor Delfs, associate professor of obstetrics, Johns Hopkins University School of Medicine, Baltimore.

Obesity, Dr. William Parson, professor of internal medicine, University of Virginia School of Medicine, Charlottesville, Va.

A Rational and Aggressive Plan for the Management of Acute Upper Gastrointestinal Hemorrhage, Dr. Charles M. Thompson, professor of medicine and head, department of gastroenterology, Hahnemann Medical College and Hospital of Philadelphia.

Modern Concepts of Toxemias of Pregnancy, Dr. Washington C. Winn, professor of clinical obstetrics and associate professor of clinical gynecology, Medical College of Virginia, Richmond, Va.

WISCONSIN

Personal.—Edmund Fitzgerald, Ph.B., LL.D., president, Northwestern Mutual Life Insurance Company, Milwaukee, has been appointed to serve on the National Advisory Health Council, the surgeon general, U. S. Public Health Service, announced Oct. 19. The council is composed of 12 nonfederal leaders in medical science and public affairs, with ex officio members from the Department of Defense and the Veterans' Administration. On the council's recommendation, the surgeon general awards grants to scientists in hospitals, universities, and other nonfederal institutions conducting research.

Symposium on Immunology.—The Milwaukee Academy of Medicine will present an all-day symposium on immunology at Marquette University, Brooks Memorial Union, Dec. 1. The faculty will include Drs. Frank J. Dixon Jr., University of Pittsburgh School of Medicine; Tzvee N. Harris, University of Pennsylvania School of Medicine, Philadelphia; William B. Sherman, Columbia University College of Physicians and Surgeons, New York; Carl V. Moore, Washington University School of Medicine, St. Louis, and Theodore L. Squier, Marquette University School of Medicine, Milwaukee. All physicians are welcome. There will be no registration fee. Luncheon will be served at the union. Reservations may be secured through the Milwaukee Academy of Medicine, 561 N. 15th St., Milwaukee 3.

WYOMING

State Medical Election.—Newly elected officers of the Wyoming State Medical Society include Drs. Joseph S. Hellewell, Evanston, president; Harlan B. Anderson, Casper, president-elect; Luther H. Wilmoth, Lander, vice-president; Benjamin Gitlitz, Thermopolis, secretary; and Carleton D. Anton, Sheridan, treasurer.

GENERAL

A. M. A. Seattle Clinical Meeting, Nov. 27-30.—Physicians who attend the Clinical Meeting in Seattle may decide which and how many of 21 panel discussions, 46 lectures and talks, 18 television clinics, 24 motion pictures, and 97 scientific exhibits they desire to attend. Much effort has been made to bring practical solutions to everyday problems with a panel discussion on office gynecology, lectures on office treatment of varicose veins and office treatment of mild depressions, and a motion picture on office management of arthritis.

The Scientific Program starts Tuesday morning and continues until Friday noon at the Civic Auditorium. On Tuesday evening, a special showing of a motion picture "The Medical Witness" will be presented at the Olympic Hotel, with introductory remarks by C. Joseph Stetler, Director, Law Department, American Medical Association; David F. Maxwell, President, American Bar Association; and David B. Allman, President-Elect, American Medical Association.

Capps Prize for Medical Research.—The Joseph A. Capps Prize for Medical Research ($300), founded by Dr. and Mrs. Edwin R. LeCount, is being offered by the Institute of Medicine of Chicago for the most meritorious investigation in medicine or in the specialties of medicine. The investigation may be also in the fundamental sciences, provided the work has a definite bearing on a medical problem. Competition for 1956 is open to graduates of Chicago medical schools who completed their internship or one year of laboratory work within five years before Jan. 1, 1956, excluding their terms of service in the armed forces. Manuscripts must be submitted to the Secretary of the Institute of Medicine of Chicago, 86 E. Randolph St., Chicago 1, not later than Dec. 31. The manuscript of the prize paper, as submitted, will become the property of the Institute of Medicine of Chicago.

Committee on Disaster Studies.—The committee on Disaster studies, of the division of anthropology and psychology, National Academy of Sciences-National Research Council (2101 Constitution Ave., Washington, D. C.), was established as the result of a request made of the academy-research council by the surgeons general of the Army, the Navy, and the Air Force, that it "conduct a survey and study in the fields of scientific research and development applicable to problems which might result from disasters caused by enemy action." The committee maintains a clearinghouse on disaster research, publishes a roster of scientific personnel in the field of disaster research, and issues a newsletter. It makes grants to encourage research in disaster studies, advises with responsible officials on problems of human behavior in disaster, and reports on the results of disaster research. Both new reports and previously unpublished work are selected for publication. Members of the committee serve without compensation beyond their actual expenses. Activities are presently supported by a grant from the Ford Foundation and by a special grant from the National Institute of Mental Health of the Department of Health, Education, and Welfare. Grants for the work of the committee are received and administered by the National Academy of Sciences. Established by Act of Congress in 1863, the academy is a private nonprofit organization of scientists dedicated to the furtherance of science and to its use for the general welfare. Pursuant to a request made by President Wilson in 1916, the academy organized the National Research Council.

FOREIGN

Swedish-American Exchange Fellowship.—The American Cancer Society in cooperation with the Anti-Cancer Society of Sweden has completed plans for a Swedish-American Exchange Fellowship program that will encourage an interchange of American and Swedish cancer research scientists.

Hadassah Establishes Health Center.—Hadassah, the Women's Zionist Organization of America, has announced as an eighth anniversary gift to the state of Israel the establishment of a Community Health Station, equipped to provide preventive, diagnostic, and curative physical and mental health services, in the all-Arab village of Abu Ghosh on the Jerusalem-Tel Aviv Highway. The new program for Abu Ghosh will include the dissemination of the latest information about health and sanitation, the breaking down of cultural or environmental taboos interfering with sound physical or emotional health, vaccination and immunization, treatment of existing physical ailments including dental and eye care, and the treatment of emotional tensions within the family group.

EXAMINATIONS AND LICENSURE

BOARDS OF MEDICAL EXAMINERS

Alabama: *Examination.* Montgomery, June 18-20. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery 4.

Arkansas:* *Examination and Reciprocity.* Little Rock, Nov. 8-9. Sec., Dr. Joe Verser, Harrisburg.

California: *Oral Examination for Reciprocity Applicants.* Los Angeles, Nov. 17. Sec., Dr. Louis E. Jones, 1020 N Street, Sacramento.

Colorado:* *Examination.* Denver, Dec. 4-5. Final date for filing application was Nov. 2. Sec., Dr. Samuel H. Brown, 831 Republic Bldg., Denver 2.

Connecticut:* *Examination.* Hartford, Nov. 13-15. Sec., Dr. Creighton Barker, 160 St. Roman St., New Haven.

Delaware: *Examination.* Dover, Jan. 8-10. *Reciprocity.* Dover, Jan. 17. Sec., Dr. Joseph S. McDaniel, 225 So. State St., Dover.

District of Columbia:* *Examination.* Washington, Nov. 13-14. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., N.W., Washington 6.

Florida:* *Examination.* Miami Beach, Nov. 25-27. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami 36.

Idaho: *Examination and Reciprocity.* Boise, Jan. 7-9. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

Iowa:* *Examination.* Des Moines, Dec. 3-5. Ex. Sec., Mr. Ronald V. Saf, State Office Bldg., Des Moines.

Kansas: *Examination and Endorsement.* Topeka, Dec. 12-13. Sec., Dr. Lyle F. Schmaus, 872 New Brotherhood Bldg., Kansas City.

Kentucky: *Examination.* Louisville, Dec. 10-12. Sec., Dr. Russell Teague, 620 South Third St., Louisville 2.

Louisiana: *Examination and Reciprocity.* New Orleans, Dec. 6-8. Sec., Dr. Edwin H. Lawson, 930 Hibernia Bank Bldg., New Orleans 12.

Maine: *Examination and Reciprocity.* Portland, Nov. 13-14. Sec., Dr. Adam P. Leighton, 192 State St., Portland.

Maryland: *Examination.* Baltimore, Dec. 11-14. Sec., Dr. Lewis P. Gundry, 1211 Cathedral St., Baltimore 1.

Massachusetts: *Examination.* Boston, Jan. 15-18. Sec., Dr. Robert C. Cochrane, State Office Bldg., Boston.

Mississippi: *Reciprocity.* Jackson, December. *Examination.* Jackson, June. Asst. Sec., Dr. R. N. Whitfield, Old Capitol, Jackson.

Nebraska:* *Examination.* Omaha, June 17-19. Director, Mr. Husted K. Watson, Room 1009, State Capitol Bldg., Lincoln 9.

New Hampshire: *Examination and Reciprocity.* Concord, March 13-14. Sec., Dr. John S. Wheeler, 107 State House, Concord.

New Mexico:* *Examination and Reciprocity.* Santa Fe, Nov. 19-20. Sec., Dr. R. C. Derbyshire, 227 East Palace Ave., Santa Fe.

North Carolina: *Reciprocity.* Charlotte, Jan. 14. Asst. Sec., Mrs. Louise J. McNeill, 716 Professional Bldg., Raleigh.

North Dakota: *Examination and Reciprocity.* Grand Forks, Jan. 2-5. Sec., Dr. C. J. Glaspel, Grafton.

Ohio: *Examination and Reciprocity.* Columbus, Dec. 18-20. Sec., Dr. H. M. Platter, 21 West Broad Street, Columbus 15.

Oklahoma:* *Reciprocity.* Oklahoma City, Dec. 7-8. *Examination.* Oklahoma City, June 11-12. Sec., Dr. E. F. Lester, 813 Braniff Building, Oklahoma City.

Oregon:* *Reciprocity and Examination.* Portland, January. Ex. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland 4.

Pennsylvania: *Examination.* Philadelphia, Jan. 7-10. Act. Sec., Mrs. Marguerite G. Steiner, Box 911, Harrisburg.

Rhode Island:* *Examination.* Providence, Jan. 3-4. Administrator, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

South Carolina: *Examination and Reciprocity.* Columbia, Dec. 11-12. Sec., Mr. N. B. Heyward, 1329 Blanding St., Columbia.

South Dakota:* *Examination.* Sioux Falls, Jan. 21-22. Ex. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

Texas:* *Examination and Reciprocity.* Fort Worth, Dec. 6-8. Applications for reciprocity must be complete and on file at least thirty days prior to the December meeting, and applications for examination must be complete and on file at least ten days prior to the meeting date. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

Utah: *Reciprocity.* Salt Lake City, Nov. 20. *Examination.* Salt Lake City, July 11-13. Director, Mr. Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

Vermont: *Examination and Reciprocity.* Burlington, Jan. 30, Feb. 1. Sec., Dr. F. J. Lawliss, Richford.

Virginia: *Examination and Reciprocity.* Richmond, Dec. 5-7. Address: Secretary to the Board, 631 First St., S.W., Roanoke.

Washington:* *Examination and Reciprocity.* Seattle, Jan. 14-16 and Jan. 12. Sec., Mr. Edward C. Dohm, Olympia.

West Virginia: *Examination.* Charleston, January. Sec., Dr. Newman H. Dyer, State Office Building No. 3, Charleston 5.

Wisconsin:* *Reciprocity.* Jan. 9. *Examination.* Madison, Jan. 8-10. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Bldg., 1 West Wilson St., Madison.

Alaska:* On application in Anchorage, Fairbanks, Juneau and other towns. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

Guam: *Subject to Call.* Act. Sec., Dr. S. F. Provencher, Agana.

Hawaii: *Examination.* Honolulu, Jan. 14-15. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Colorado: *Examination and Reciprocity.* Dec. 5-6, Lincoln and Denver. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

Florida: *Examination.* Gainesville, Nov. 10. Sec., Dr. M. W. Emmel, University of Florida, Box 340, Gainesville.

Oklahoma: *Examination.* Oklahoma City, April 19-20. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.

Oregon: *Examination.* Portland, Dec. 1. Dr. Earl M. Palett, Sec., State Board of Higher Education, Eugene.

South Dakota: *Examination.* Vermillion, Dec. 7-8. Sec., Dr. Gregg M. Evans, 310 E. 15th St., Yankton.

Washington: *Examination.* Seattle, Jan. 9-10. Sec., Mr. Edward C. Dohm, Olympia.

Wisconsin: *Examination.* Milwaukee, Dec. 1 and April 6. Sec., Dr. W. H. Barber, 621 Ransom St., Ripon.

Alaska: *Examination and Reciprocity.* Anchorage and Juneau, first week of February, April, June, August and November. Sec., Dr. C. Earl Albrecht, Box 1931, Juneau.

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*Basic Science Certificate required.

GOVERNMENT SERVICES

ATOMIC ENERGY COMMISSION

AEC Awards Research Contracts.—The U. S. Atomic Energy Commission has announced the award of 20 unclassified life science research contracts in the fields of medicine and biology to universities and private institutions. In the medical sciences eight contract renewals for one year were awarded to allow for continuation of research already in progress. The following new contracts were awarded:

Cedars of Lebanon Hospital, Los Angeles: Chemical Studies on Connective Tissues of Animals Aged Prematurely by *Irradiation* (Assessment of Biochemical Age), Harry Sobel, Ph.D.

University of Colorado, Denver: A Study of the Combined Action of Certain Chemical Inhibitors of Metabolism with X-Radiation and Other Ionizing Radiations on the Growth of *Certain* Transplantable Malignant Tumors, Richard W. Whitehead and Raymond R. Lanier.

University of Illinois, Chicago: A Study on the *Effects* of Intragastric Irradiation with Beta Rays from Ruthenium^{106}–Rhodium^{106} in Patients with Malignant Disease, Armand Littman.

AIR FORCE

Air Force Residency Training.—Since July 1, 1956, a total of 180 U. S. Air Force physicians have entered residency training. Of this number, 154 are receiving their training in civilian hospitals and 26 are in training in military hospitals. At present, 23 physicians have been approved for residency training beginning in 1957, 14 in civilian hospitals and 9 in military hospitals. The Air Force has openings in almost all the clinical specialties for residency training beginning in July, 1957. In addition, a total of 155 Air Force physicians are taking sponsored internships, 96 in civilian hospitals and 59 in military hospitals.

NAVY

Rear Admiral Pugh Accepts University Position.—Rear Adm. Lamont Pugh, retired, surgeon general of the Navy from 1951 to 1955, has accepted a position as university physician at George Washington University, Washington, D. C. In his new position, he will deal mostly with the ailments that may beset the university students. Admiral Pugh was also commanding officer of the Naval Medical Center at Bethesda, Md., prior to his recent retirement from active service.

PUBLIC HEALTH SERVICE

Fluoridated Water Supplies.—The Public Health Service reported on Oct. 28 a marked increase in the number of people drinking fluoridated water to help protect children's teeth against decay. The latest tabulation shows that fluoridated drinking water is now furnished in this country to one-fourth of the people using public water supplies. During the first nine months of 1956, communities with a combined population of 6 million started fluoridating their water. In 1946 fluoridation was used in only 12 communities with a total population of 328,000. About 1,400 cities and towns with a total population of over 30 million people were using fluoridation at the end of September, 1956. Among the larger cities adopting this preventive dental health measure are Chicago; Philadelphia; Baltimore; Washington, D. C.; Pittsburgh; Cleveland; Milwaukee; San Francisco; St. Louis; and Buffalo.

Establish Center for Aging Research.—The Surgeon General, Dr. Leroy E. Burney, has announced the establishment of a Center for Aging Research in the National Institutes of Health, of which Dr. G. Halsey Hunt, at present associate chief of the Public Health Service bureau of medical services, has been appointed director.

The new center is a part of the Public Health Service's program to coordinate and accelerate all of its activities in the field of aging. The primary objective of the new program is to support additional research into the mechanisms involved in aging. A first activity will be to aid universities, medical schools, and other research organizations in establishing comprehensive research centers on aging, to be supported in part by research grants from the National Institutes of Health.

Creation of a Center for Aging Research in the Public Health Service is in line with the program developed by the federal government through the Federal Council on Aging and the member departments and agencies to coordinate all activities associated with the problem of aging.

Marion B. Folsom, Secretary of Health, Education, and Welfare, said, "There are more than 12 million people in this country today who are over the age of 65; by 1970, there will be more than 18 million. Many of our older citizens have special health problems. It is important that more be done to help solve these problems—to help older persons to greater independence and self-sufficiency and a life more free of disease and disability."

New Director of Clinical Center.—The surgeon general has announced the assignment of Dr. Jack Masur, Washington, D. C., as director of the Clinical Center at the National Institutes of Health in Bethesda, Md. Dr. Masur, who supervised the planning and building of the Clinical Center, assumed his new duties Nov. 1. The Clinical Center, which is said to be the largest facility of its kind in the world for research in the major diseases, was officially opened in July, 1953, and present facilities are about to be expanded to permit more research in neurological and cardiac surgery. Nearly 5,000 patients from all over the United States have been admitted to the center for study and treatment. It is the responsibility of the director of the Clinical Center to plan and use the facility so that patients will receive the best in medical care and, at the same time, the research programs will be carried forward with maximum effectiveness. Dr. Masur, a native of Augusta, Ga., entered the commissioned corps of the Public Health Service in 1943. Since 1951 he has been chief of the bureau of medical services in the surgeon general's office. He is president of the American Association of Hospital Consultants, a trustee of the American Hospital Association, and a member of the Joint Commission on Accreditation of Hospitals.

Four-Year Study of Cerebral Palsy and Mental Retardation.—Awards of more than $700,000 for a four-year study of the causes of cerebral palsy and mental retardation have been made to Yale University School of Medicine, New Haven, Conn., and to Brown University, Providence, R. I., the surgeon general of the Public Health Service has announced. These awards mark the beginning of a research program that, during the next 10 to 20 years, will attempt to identify factors responsible for cerebral palsy, mental retardation, blindness, and deafness.

Brown and Yale universities are the first of a dozen or more institutions that are expected to join this program. Yale's grant for the first year is $107,799; Brown's is $97,633. The surgeon general said plans contemplate that more than 1 million dollars yearly will be awarded to medical institutions under the program of the National Institute of Neurological Diseases and Blindness.

When the full roster of participating medical institutions has been achieved, it is expected that more than 6,000 persons will be studied annually. Mothers, infants, and children will be studied over a period of several years. The data to be collected by the participating medical institutions will include complete family history, pregnancy and prenatal histories, a detailed account of events at birth, and a complete physical and psychological history of each child during his initial stay at the hospital. Infants who show signs of stress, defects in development, or neurological problems will be selected for follow-up and will receive periodic psychological and neurological examinations. It is expected that these studies will clarify the role of heredity, brain injury and brain hemorrhage, lack of oxygen, difficulty in breathing, prenatal and postnatal infections, and anemia of the newborn in the development of neurological disorders.

The National Institute of Neurological Diseases and Blindness of the National Institutes of Health will analyze all data obtained by the cooperating medical centers and will submit the findings to each participating institution. The study at the Yale University School of Medicine will be under the general direction of Dr. Gilbert H. Glaser, and the project at Brown University will be directed by Dr. Eric Denhoff.

DEATHS

Elliott, B. Landis ✠ Kansas City, Mo.; born in St. Louis Dec. 18, 1890; Washington University School of Medicine, St. Louis, 1919; associate clinical professor of medicine (neurology) at the University of Kansas School of Medicine, Kansas City, Kansas: specialist certified by the American Board of Psychiatry and Neurology; past-president of the Jackson County Medical Society, and in 1942 received that organization's merit award for outstanding service to the Community Health League of Missouri: in 1936 vice-president of the Central Neuropsychiatric Association: in 1931 secretary, and in 1932 president, of the Missouri-Kansas Neuropsychiatric Society: vice-chairman, Section on Nervous and Mental Diseases, 1936-1937, American Medical Association; fellow of the American Psychiatric Association; member of the Kansas City Academy of Medicine, Kansas City Southwest Clinical Society, and the Missouri Society for Neurology and Psychiatry; served as chief of staff, St. Joseph Hospital, and head of the psychiatric department, St. Mary's Hospital; member of the staffs at St. Luke's, Trinity Lutheran, Menorah, Neurological, Research, and Kansas City General hospitals; in 1920 was with the Red Cross in Finland, and for this service was awarded the Order of the White Rose by the government of Finland; died in Lisbon, Portugal, Sept. 8, aged 65, of coronary thrombosis, while on a vacation in Europe.

Walsh, Jeremiah Henry ✠ Corning, N. Y.; born in Curtis, N. Y., Aug. 6, 1870; Niagara University Medical Department, Buffalo, 1894; an associate member of the American Medical Association, serving as a member of its House of Delegates from 1917 to 1924, a trustee from 1924 to 1933, and for many years secretary of the Board of Trustees; president of the Chicago Medical Society, 1924-1925; member of the Illinois State Medical Society; for many years practiced in Chicago, attending surgeon at the City of Chicago Municipal Tuberculosis Sanitarium, St. Anne's Hospital, and Norwegian-American Hospital, and consulting surgeon, St. Anthony de Padua Hospital: during World War I member of the exemption board, Selective Service; at one time a member of the board of education of Chicago; died Oct. 12, aged 86, of arteriosclerosis.

Muller, Henry Richard, Pittsfield, Mass.; Cornell University Medical College, New York City, 1913; at one time taught pathology at Johns Hopkins University in Baltimore; formerly associated with the Rockefeller Institute in New York City: served on the staffs of St. Luke's Hospital in Cleveland, Vassar Brothers Hospital in Poughkeepsie, N. Y., and the Doctors Hospital in New York City; on the staffs of the W. B. Plunkett Memorial Hospital in Adams and the Hillcrest Hospital, where he died Aug. 18, aged 69, of prolonged effects of injuries received in an automobile accident.

Alexander, Joseph H. ✠ Zavalla, Texas; Memphis (Tenn.) Hospital Medical College, 1891; an honorary staff member of Angelina County Hospital and Memorial Hospital, Lufkin: examining surgeon for the Southern Pacific Lines in Texas and Louisiana; died in Cleveland Aug. 25, aged 86, of coronary thrombosis.

Arkin, Archie Abraham ✠ Des Moines, Iowa; University of Manitoba Faculty of Medicine, Winnipeg, Manitoba, Canada, 1932; member of the American Academy of General Practice: on the staffs of Mercy and Iowa Lutheran hospitals; died in St. Mary's Hospital, Rochester, Minn., Aug. 14, aged 55, of pulmonary edema and myocardial infarction.

Baker, Cecil Heber ✠ St. Louis: St. Louis University School of Medicine, 1910; veteran of World War I; on the staff of the Lutheran Hospital: died Sept. 4, aged 69, of coronary thrombosis.

Barrett, Van F. ✠ Lakeview, Ohio: Western Reserve University Medical Department, Cleveland, 1895; died in the Mary Rutan Hospital, Bellefontaine, Aug. 31, aged 87, of coronary thrombosis.

Bentley, Norman Philip ✠ St. Paul; Syracuse University College of Medicine, Syracuse, N. Y., 1909: member of the American Academy of General Practice; veteran of World War I; died Aug. 6, aged 68, of carcinoma of the lung.

Borow, Henry ✠ Bound Brook, N. J.: University of Arkansas School of Medicine, Little Rock, 1931; one of the founders and staff member of the Bound Brook Hospital, where he was a member of the board and where he died Sept. 9, aged 51, of lymphosarcoma.

Carter, Ross Stagg, San Diego, Calif.: Johns Hopkins University School of Medicine, Baltimore, 1910: past-president of the San Diego County Medical Society; died Aug. 26, aged 73, of pulmonary emphysema and heart disease.

Collinson, Thomas Jefferson ✠ Tupper Lake, N. Y.; Queen's University Faculty of Medicine, Kingston, Ontario, Canada, 1908; died in the Royal Victoria Hospital, Montreal, Quebec, Canada, Aug. 14, aged 73, of myocardial infarction.

Curtis, Stephen Horace ✠ Troy, N. Y.: Albany (N. Y.) Medical College, 1915; in 1946 member of the House of Delegates of the American Medical Association, member of the American Society of Clinical Pathologists; fellow of the American College of Physicians; on the staffs of the Leonard and Samaritan hospitals; died Aug. 20, aged 62, of coronary occlusion.

Devol, Edmund, New York City; New York Homeopathic Medical College and Hospital, New York City, 1896; an associate member of the American Medical Association; died in the Roosevelt Hospital Aug. 28, aged 83.

Doran, William Thomas, New York City; Long Island College Hospital, Brooklyn, 1905; fellow of the American College of Surgeons; formerly on the faculty of University and Bellevue Hospital Medical College: an associate member of the American Medical Association; surgical director of Columbus Hospital; for many years on the staff of Bellevue Hospital; died in the Metropolitan Hospital Sept. 10, aged 78, of injuries received in an automobile accident.

Douglas, George R. ✠ Valparaiso, Ind.: the Hahnemann Medical College and Hospital, Chicago, 1901; for many years county health officer; served as health officer of Valparaiso; past-president of the Porter County Medical Society; on the staff of the Porter Memorial Hospital, where he died July 8, aged 82, of coronary occlusion.

Duggan, LeRoy Bates ✠ Houston, Texas; University of Texas School of Medicine, Galveston, 1928; clinical associate professor of medicine, Baylor University College of Medicine; specialist certified by the American Board of Internal Medicine; member of the American College of Gastroenterology and the American Psychosomatic Society; fellow of the American College of Physicians; veteran of World War II; on the staff of Hermann Hospital, where he died Aug. 27, aged 55.

Foster, Daniel Parsons, Detroit; Harvard Medical School, Boston, 1922; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; an associate member of the American Medical Association; for many years head of the division of metabolic diseases at Henry Ford Hospital, where he died Aug. 21, aged 64, of bronchopneumonia.

Foust, Earl Harland ✠ Eustis, Fla., University of Michigan Department of Medicine and Surgery, Ann Arbor, 1904; member of the Michigan State Medical Society; died Aug. 27, aged 78, of pneumonia.

Ginsburg, Abraham ✠ New York City; Long Island College Hospital, Brooklyn, 1910; veteran of World War II; died Aug. 23, aged 68.

Glass, Bernard Robert, Napa, Calif.; Creighton University School of Medicine, Omaha, 1937; interned at the U. S. Marine Hospital, San Francisco; senior physician and surgeon on the staff of the Napa State Hospital in Imola; died in the Parks Victory Memorial Hospital Sept. 3, aged 45, of hemorrhage due to peptic ulcer.

✠ Indicates Member of the American Medical Association.

Golley, Kyle Wood ⊕ Baltimore; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1921; on the staffs of St. Joseph's Hospital and the Mercy Hospital, where he died Sept. 6, aged 59, of cerebral hemorrhage.

Gordon, Adolphus Noble, Chicago; Meharry Medical College, Nashville, Tenn., 1894; on the staff of the Provident Hospital; died in the Albert Merritt Billings Hospital Sept. 22, aged 85, of post prostatectomy hemorrhage.

Guajardo, Javier G., Laredo Texas (licensed in Texas in 1926), died Aug. 21, aged 92, of bronchopneumonia and arteriosclerotic heart disease.

Hampton, John Erwin ⊕ Newport, Tenn.; University of Tennessee Medical Department, Nashville, 1902; veteran of World War I and the Spanish-American War; died in the Valentine-Shults Hospital Sept. 2, aged 78, of nephritis and heart disease.

Hankins, Thornton Wilson ⊕ Swoope, Va.; Medical College of Virginia, Richmond, 1906; died Aug. 31, aged 74, of cerebral embolism and arteriosclerosis.

Hasner, Robert Bain ⊕ Royal Oak, Mich.; Rush Medical College, Chicago, 1908; past-president of the Oakland County Medical Society; an honorary staff member of the board of Highland Park (Mich.) General Hospital; served on the executive medical board of the William Beaumont Hospital, where he died Sept. 16, aged 72, of cerebral thrombosis.

Heaton, Thomas Henry ⊕ Cambridge, Mass.; Tufts College Medical School, Boston, 1898; died Aug. 4, aged 81, of cerebral hemorrhage.

Henry, Albert Cleaver ⊕ Wickford, R. I.; Hahnemann Medical College and Hospital of Philadelphia, 1930; past-president of the Washington County Medical Society; served as president of the staff of South County Hospital in Wakefield, and the Roger Williams General Hospital in Providence; school physician; died Aug. 15, aged 52, of coronary occlusion.

Hill, Reginald Lindsey, Lyndonville, Vt.; University of Vermont College of Medicine, Burlington, 1923; served as health officer; on the staff of the Brightlook Hospital in St. Johnsbury; died Aug. 9, aged 57, of heart disease.

Horrigan, Thomas Francis ⊕ Detroit; Wayne University College of Medicine, Detroit, 1945; interned at the City of Detroit Receiving Hospital; formerly a resident at the Providence Hospital; served in the Medical Corps, Army of the United States; on the staff of the Metropolitan Hospital; died in Oscoda Aug. 13, aged 36, of coronary thrombosis.

Howard, Isaac B. ⊕ Williamson, Ga.; Atlanta School of Medicine, Atlanta, 1909; for many years member of the county board of education; died Aug. 10, aged 81, of coronary thrombosis.

Howell, William Erastus ⊕ Morristown, Tenn.; Tennessee Medical College, Knoxville, 1903; past-president of the Tennessee Medical Association; died Aug 28, aged 76.

Hubbard, Ralph George, Detroit; University of Michigan Medical School, Ann Arbor, 1926; an associate member of the American Medical Association; served on the faculty of his alma mater, on the staffs of the Woman's and Florence Crittenden hospitals, and the Mount Carmel Mercy Hospital, where he died Aug. 31, aged 57, of arteriosclerosis.

Jameson, Robert Emmet ⊕ Phoenix, Ariz.; Milwaukee Medical College, Milwaukee, 1912; member of the Iowa State Medical Society; for many years practiced in Davenport, Iowa, and was secretary of the Scott County Medical Society; died Aug. 12, aged 76, of asthmatic bronchitis and emphysema.

Jenkins, Charles Rivington, Daytona Beach, Fla.; Long Island College Hospital, Brooklyn, N. Y., 1899; member of the Medical Society of the State of New York; died July 8, aged 77, of reticulum cell sarcoma.

Johnston, George P. ⊕ Cheyenne, Wyo.; Medical College of Ohio, Cincinnati, 1891; member of the House of Delegates of the American Medical Association, 1903, 1917-1918, 1923, 1926-1929, 1931, 1933-1935, and 1937-1948; fellow of the International College of Surgeons and the American College of Surgeons; died Sept. 18, aged 93, of heart disease.

Jordan, Thomas Cook, Jr. ⊕ Milledgeville, Ga.; Medical College of Georgia, Augusta, 1945; member of the Medical Association of Georgia and the American Academy of General Practice; formerly an officer in the Medical Corps, Army of the United States, died Aug. 13, aged 39, of coronary thrombosis.

Kaplan, Maurice Isadore ⊕ Chicago; Washington University School of Medicine, St. Louis, 1910; assistant professor of radiology at the Chicago Medical School; member of the Radiological Society of North America; from 1914 to 1921 health officer, department of health; for many years on the staff of the Mount Sinai Hospital, where he died Sept. 6, aged 68, of pyelonephritis and diabetes mellitus.

Katzoff, Manuel, Norfolk, Va.; Baltimore Medical College, Baltimore, 1906; died in the Leigh Memorial Hospital Aug. 14, aged 71, of cancer of the stomach,

Keating, Francis Raymond, Philadelphia; Medico-Chirurgical College of Philadelphia, 1905; an associate member of the American Medical Association; for many years a medical referee for the Prudential Insurance Company; died in the Pennsylvania Hospital Sept. 9, aged 76, of heart disease.

Kellogg, Frederic Sherlock, Oxford, Miss.; University of Pennsylvania Department of Medicine, Philadelphia, 1897; member of the Medical Society of the State of Pennsylvania; an associate member of the American Medical Association, for many years practiced in Pittsburgh, where he was on the staff of the Western Pennsylvania Hospital; served as a member of the Lenawee County (Mich.) draft board; died in the Oxford Hospital July 31, aged 84, of heart disease.

Kidder, Frank Woodman Kinsman, Los Angeles, College of Physicians and Surgeons, Los Angeles, 1909, an associate member of the American Medical Association; specialist certified by the American Board of Radiology, member of the Radiological Society of North America and the American College of Radiology; died in the Hospital of the Good Samaritan Aug. 1, aged 69, of coronary heart disease and arteriosclerosis.

Kirov, Konstantin Vesselin ⊕ Chicago; Leopold Franzens-Universitat Medizinische Fakultät, Innsbruck, Austria, 1947; died in the Wesley Memorial Hospital July 27, aged 33, of Hodgkin's disease.

Knoch, Norbert Henry ⊕ Glenwood Springs, Colo ; Denver and Gross College of Medicine, Denver, 1910, on the staffs of St Joseph's and Childrens hospitals in Denver, and the Valley View Hospital; died July 27, aged 67, of heart disease.

Krieger, Henry Arthur, Madison, S. D., Bennett Medical College, Chicago, 1909; died June 27, aged 74, of cerebral thrombosis and diabetes mellitus.

Langley, John Wesley, Granby, Mo.; College of Medicine and Surgery (Physio-Medical), Chicago, 1890, died Aug 17, aged 89, of coronary disease.

Lavin, Francis Charles ⊕ Carbondale, Pa.; Georgetown University School of Medicine, Washington, D. C, 1932, veteran of World War II; associated with St. Joseph's Hospital, where he died Aug. 10, aged 50, of a heart attack.

Leeson, Ernest Edward, Inverness, Fla., College of Physicians and Surgeons of Chicago, 1894; died in the Veterans Administration Hospital, Bay Pines, July 6, aged 84, of arteriosclerotic heart disease.

Lewi, William Grant, Glendale, Calif.; Albany (N. Y.) Medical College, 1892, an associate member of the American Medical Association; member of the Medical Society of the State of New York; died Aug. 18, aged 86, of cerebral vascular accident.

Llewellyn, Charles Elroy ⊕ Richmond, Va.; Medical College of Virginia, Richmond, 1916; member of the American Academy of General Practice; on the staff of the Johnston-Willis Hospital, died while on a vacation, Aug. 24, aged 63, of injuries received in an automobile accident near Parlin, Colo.

McClendon, John Irvin, Russell Springs, Ky.; University of Louisville Medical Department, Louisville, 1907, died Aug. 3, aged 76.

McCracken, Earl Joseph ⊕ Whittier, Calif.; University of Louisville (Ky.) School of Medicine, 1947; interned at the Kentucky Baptist Hospital in Louisville, Ky.; served in the U. S. Air Force Reserve; on the staff of the Beverly Community Hospital in Montebello; died July 17, aged 42, of arteriosclerosis.

McGuire, Frank James ✠ Guilford, Conn.; Boston University School of Medicine, Boston, 1937; veteran of World War II; served on the staff of Hospital of St. Raphael in New Haven; died Sept. 1, aged 46, of sarcoma of the lung.

McKenna, Joseph Lawrence ✠ Grand Rapids, Mich.; University of Michigan Medical School, Ann Arbor, 1926; veteran of World War II; served on the staff of St. Mary's Hospital; died Aug. 25, aged 54, of pulmonary embolism.

Martin, John Reboe Bitner, Gap, Pa.; Miami Medical College, Cincinnati, 1903; died Aug. 21, aged 75, of acute coronary occlusion.

Meeker, Irving Avard, Upper Montclair, N. J.; New York Homeopathic Medical College and Hospital, New York City, 1898; an associate member of the American Medical Association; medical examiner, board of education, town of Montclair; died at Columbia-Presbyterian Medical Center, New York City, Sept. 15, aged 83, of cerebral thrombosis.

Melchiorre, Nicholas Vincent ✠ Philadelphia; Temple University School of Medicine, Philadelphia, 1930; on the staff of St. Agnes Hospital, where he died Aug. 28, aged 50, of acute myocardial infarction.

Meyers, Lloyd Rogers, Cumberland, Md.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1915; member of the Medical and Chirurgical Faculty of Maryland; on the staffs of the Memorial and Sacred Heart hospitals; died Aug. 11, aged 65, of coronary thrombosis.

Miller, Lewis Israel ✠ Denver; Loyola University School of Medicine, Chicago, 1918; served as president of the Colorado Hospital Service; on the staffs of the Beth Israel, St. Anthony, and Childrens hospitals; died Aug. 13, aged 61, of acute coronary thrombosis.

Morgan, Burnice Earl ✠ Asheville, N. C.; University of Tennessee College of Medicine, Memphis, 1917; member of the American Academy of General Practice; for many years chairman of the Buncombe County Board of Education; past-president of the Buncombe County Medical Society and of the Tenth District Medical Society; veteran of World War I; on the staffs of the St. Joseph's, Aston Park, and the Memorial Mission hospitals; for a time a member of the board of trustees of Asheville-Biltmore College; died Aug. 14, aged 62.

Morgan, Loftus E., Baton Rouge, La.; Trinity Medical College, Toronto, Ontario, Canada, 1890; died at Our Lady of the Lake Hospital Aug. 21, aged 91, of coronary occlusion.

Neff, Robert Lee ✠ Joplin, Mo.; University Medical College of Kansas City, Mo., 1894; an associate member of the American Medical Association; fellow of the American College of Surgeons; on the staff of St. John's Hospital, where he died Aug. 23, aged 86, of coronary occlusion.

Orton, George Lee, Rahway, N. J.; Jefferson Medical College of Philadelphia, 1909; an associate member of the American Medical Association; past-president of the Union County Medical Society; formerly member of the board of health; on the staff of the Rahway Memorial Hospital of which he was a founder; died Aug. 11, aged 78, of coronary artery disease and heart block.

Payne, Richard Johnson ✠ St. Louis; St. Louis University School of Medicine, St. Louis, 1913; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; on the staffs of the Barnes, St. Louis Children's, and Missouri Baptist hospitals; died Aug. 28, aged 68, of coronary occlusion.

Rand, Paul King, Alexandria, La.; Tulane University School of Medicine, New Orleans, 1913; past-president of the Louisiana State Medical Society, of which he was a member; veteran of World War I; at one time on the faculty of the University of Wisconsin in Madison; past chief of staff, Baptist Hospital; on the staff of St. Frances Cabrini Hospital; died Aug. 7, aged 68, of heart disease.

Rayhill, John Wayland, Utica, N. Y.; Long Island College Hospital, Brooklyn, 1906; served on the staff of the Faxton Hospital, where he died Aug. 8, aged 79.

Robinson, William Herbert, Roaring Spring, Pa.; College of Physicians and Surgeons, Baltimore, 1907; died in Altoona June 28, aged 74, of arteriosclerotic heart disease.

Rogers, James Virgil ✠ Cairo, Ga.; Emory University School of Medicine, Emory University, 1921; member of the Grady County School Board; member of the American Academy of General Practice; died in Thomasville Aug. 25, aged 64.

Saunders, Robert Ritchie, Philadelphia; Jefferson Medical College of Philadelphia, 1892; an associate member of the American Medical Association; specialist certified by the American Board of Ophthalmology; died in the Jefferson Medical College Hospital Aug. 19, aged 84.

Schutzman, Benjamin Maxwell, Detroit; Detroit College of Medicine and Surgery, Detroit, 1930; died July 24, aged 50.

Seibert, David Allen, Los Angeles; Barnes Medical College, St. Louis, 1909; formerly associated with the U. S. Veterans Bureau; died in the Veterans Administration Hospital Aug. 7, aged 74, of pneumonia.

Sharkis, David, Philadelphia; Hahnemann Medical College and Hospital, Philadelphia, 1932; on the staff of the Hahnemann Medical College and Hospital; died in the Albert Einstein Medical Center, Northern Division, Aug. 20, aged 63, of hypertension.

Sharp, Jacob Sevier, La Follette, Tenn.; Tennessee Medical College, Knoxville, 1899; died Aug. 25, aged 84, of heart disease.

Simpson, Russell Edwin, Jr. ✠ Pasadena, Calif.; Stanford University School of Medicine, San Francisco, 1942; member of the American Psychiatric Association; veteran of World War II; on the staff of the Collis P. and Howard Huntington Memorial Hospital; died Aug. 6, aged 40.

Sims, Wayne Waldo Conway ✠ Seattle; University of Colorado School of Medicine, Denver, 1929; specialist certified by the American Board of Preventive Medicine; member of the American Academy of Dermatology and Syphilology; clinical assistant professor of public health and preventive medicine at the University of Washington School of Medicine; veteran of World War II; director of the venereal disease division of the Seattle-King County Department of Health; died Aug. 23, aged 52.

Smiley, Henry Chandler, Redondo Beach, Calif.; Denver and Gross College of Medicine, Denver, 1905; formerly practiced in Torrance, where he organized the Torrance District Health Center, which he served; died in Los Angeles July 15, aged 74, of heart disease.

Sneidman, George Irving ✠ Hartford, Conn.; Medical College of Virginia, Richmond, 1936; veteran of World War II; member of the American Academy of General Practice; on the staff of the Mount Sinai Hospital; died in the Hartford Hospital Aug. 23, aged 57.

Soper, Richard Watts, Hendersonville, N. C.; Sioux City College of Medicine, Sioux City, Iowa, 1898; formerly on the staff of the Veterans Administration Hospital in Augusta, Ga.; died in the Swannanoa unit of the Veterans Administration Hospital in Oteen Sept. 1, aged 87, of carcinoma of the prostate.

Thornton, Mary Bickings ✠ Philadelphia; Woman's Medical College of Pennsylvania, Philadelphia, 1904; emeritus professor of anatomy at her alma mater; member of the American Academy of General Practice; died in the Hospital of the Woman's Medical College of Pennsylvania Sept. 7, aged 75.

Thurston, Asa, Taylorsville, N. C.; University of Maryland School of Medicine, Baltimore, 1909; member of the Medical Society of the State of North Carolina; served in the state legislature; on the staff of the Alexander County Hospital; died in the Rowan Memorial Hospital, Salisbury, Aug. 24, aged 73, of arteriosclerosis.

Warinner, Junius Ernest ✠ Richmond, Va.; Johns Hopkins University School of Medicine, Baltimore, 1916; served overseas during World War I; member of the Richmond Academy of Medicine; for many years on the staff of the Grace Hospital; member of the board of directors of the Richmond Memorial Hospital; died Sept. 4, aged 64, of a heart attack.

Way, Lewis Richard, Traverse City, Mich.; Northwestern University Medical School, Chicago, 1922; veteran of World War II; died July 8, aged 58, of myocardial infarction and coronary arteriosclerosis.

FOREIGN LETTERS

BELGIUM

Poliomyelitis.—The Minister of Public Health and Family appointed a permanent commission of experts in poliomyelitis to consider the problems concerning this disease. As compared with the United States, with its annual morbidity rate in the last 10 years varying from 18 to 37 cases per 100,000 inhabitants, the morbidity rate during this same period in Belgium was from 3 to 11 cases per 100,000 inhabitants. A serologic survey was conducted to determine what age groups are most susceptible as a guide to a rational vaccination program.

Physicians and the Government.—The conflict between government and physicians reached a culmination, and the government's attempt to establish socialized medicine was thwarted. More than 80% of the physicians refused to obey the directions according to which the forms of the official social insurance should be used. Establishing a strictly medical organization in opposition to the governmental organization of sickness insurance, the Belgian Medical Federation on Oct. 1 established the National Service of Physicians. The physicians have refused to become mere clerks. The aim of the National Service of Physicians is to assure that all persons with modest income receive the necessary medical care, with their personal rights taken into consideration. The members of this association agree to respect the scale of fees established by the National Medical Service. The beneficiaries of the National Medical Service are all persons, whether insured or not, whose yearly gross income does not exceed 100,000 francs, with an increase of 25,000 francs for a wife and 10,000 francs for each additional dependent. By means of this purely medical association and without governmental interference, the medical needs of the population will be met.

Tuberculous Meningitis.—Durieu and co-workers reported to the Belgian Society of Scientific Studies that 87 patients with tuberculous meningitis, in 65 of whom the diagnosis was bacteriologically confirmed, were given intraspinal injections of streptomycin every day for three months and then injections every two days for three additional months. Intramuscular injections were then given for six months. The patients who did not respond to this treatment were given suboccipital or intraventricular injections. There were 42 survivors with a follow-up period of two to six years. Eight patients had relapses, and 4 of these recovered; 23 of the survivors were able to resume their work. Complete deafness was observed in 9 and severe disturbances of the labyrinth in 12 patients.

FRANCE

Hepatosiderosis in Alcoholics.—J. Lereboullet and co-workers, at the meeting of the Medical Society of the Hospitals of Paris on June 29, stated that hepatosiderosis is especially frequent in alcoholics (50%) and still more so in those with chronic hepatic cirrhosis (66%). Nevertheless, 35% of the patients with hepatosiderosis are not alcoholics and have livers that are histologically normal. The authors stress the fact that massive hepatosiderosis is found in an almost constant proportion of the population irrespective of the presence of cirrhosis or alcoholism but occurs more frequently in men. Such patients also have an excess of ferric pigments in the spleen, pancreas, myocardium, kidneys, and testes. It is not known whether this represents an early stage of diffuse hemochromatosis.

Idiopathic Auricular Fibrillation.—Maurice and co-workers, at a meeting of the Medical Society of the Hospitals of Paris on June 15, reported a series of 90 patients with idiopathic auricular fibrillation. The fibrillation was poorly tolerated in 85 of the patients in that, in addition to various functional disturbances, it gave rise to cardiac insufficiency in 34 patients, to left ventricular or global hypertrophy in 57, and to electrocardiographic anomalies in 38. The cardiac index was generally diminished, and in some patients this diminution was extreme. After digitalization, stabilization with quinidine under cover of anticoagulants was attempted in 68 patients and was successful in 47. In most of these there was no recurrence of the fibrillation. The return to sinus rhythm almost invariably led to spectacular improvement and almost always to a complete disappearance of the functional disturbances and the cardiac insufficiency and even of the radiological and electrocardiographic anomalies. On the other hand, the condition of the patients whose fibrillation continued generally deteriorated. It is therefore justifiable to make a cautious attempt to stabilize idiopathic auricular fibrillation with quinidine.

Brachyesophagus.—E. Roviralta, at the meeting of the Society of Pediatrics of Montpellier on April 23, showed that, for reasons principally anatomic and clinical, brachyesophagus in the nursling is almost always acquired. Its prevention should be based on a periodic examination of children presenting partial thoracic displacement of the stomach who are undergoing medical treatment. Gastric retention should be corrected by pylorotomy or section of adhesions. Phrenicectomy has been used successfully in the hemorrhagic form. Transhiatal fixation of the cardia should be reserved, as a prophylactic measure, for patients in whom gastric drainage or paralysis of the diaphragm has failed or for those in whom there are special indications.

Hypoproteinemia.—At the same meeting, J. Chaptal and co-workers said that hypoproteinemia in infants results in severe malnutrition, severe hepatic steatosis, and a decline in serum albumin and gamma globulin levels. Treatment is difficult, and the course is often unfavorable. The lack of certain amino acids interferes with the synthesis of many digestive, hepatic, and renal enzymes and gives rise to disturbances of pigmentation, xerophthalmia, perleche, and erythredema polyneuropathy. Chromatographic study of the blood and the urine demonstrates extreme plasma deficiency of amino acids and polyaminoaciduria linked apparently to an acquired enzyme disturbance of the renal tubule. In the course of hypoproteinemia due to hepatitis, a drop in the albumin level is associated with an increased gamma globulin level. The blood and urinary chromatograms show an abundance of amino acids poorly used by the altered liver in the plasma and a suprarenal polyaminoaciduria. In one patient with essential hypoproteinemia, the nitrogen balance was positive but inadequate. The balance was maintained only when 600 mg. of protein per kilogram of weight was given intravenously every day. The child died of shock after a transfusion. In both deficiency hypoproteinemia and essential hypoproteinemia, the protein deficiency was estimated at about 10 gm. of protein per kilogram of body weight.

Renal Diabetes.—M. Bernheim and co-workers (*Pédiatrie* 11:161, 1956) state that renal diabetes is a rare constitutional disease characterized by glycosuria without hyperglycemia, a normal glucose tolerance test, and absence of any disorders in urinary elimination of phosphorus and amino acids. True renal diabetes is characterized by a lowering of the Tm_G (maximum tubular excretory capacity for glucose) and abnormal glomerular filtration; pseudorenal diabetes occurs in subjects with a normal Tm_G. The possibility of a transformation of renal diabetes into diabetes mellitus, though improbable, requires further and prolonged observation of the cases.

Idiopathic Renal Acidosis.—Jeune and Charrat (*Pédiatrie* 11:295, 1956) state that idiopathic renal acidosis is of interest clinically because it corresponds to a certain number of cases of readily curable abiotrophy in infants, and theoretically because it poses the problem of the renal mechanisms in acidobasic regulation. No cause can be recognized with certainty, but one must think either of a particular sensitivity to vitamin D or of an immaturity of the renal tubules. The clinical aspect is most frequently that of a persistent anorexia and an arrest in growth occurring after the

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The items in these letters are contributed by regular correspondents in the various foreign countries.

age of 6 months, with sudden episodes of acidosis. There is a discrepancy between blood acidosis and urinary alkalosis. The latter seems to be due to the incapacity of the proximal tubules to reabsorb bicarbonate ions, the functions of the distal tubules remaining intact.

Cystinuria.—C. A. Schiavini (*Pédiatrie* 11:181, 1956) states that modern methods of investigation of amino acid metabolism allow a differentiation between early cystinuria (or preferably lysinocystinuria) and cystinosis. Cystinosis, a rare disease, is recognized in infants by anorexia, arrest of growth, thirst, bouts of fever, and rickets, and in its late form by dwarfism, vitamin-resistant rickets, photophobia, and chronic renal disease. Hypophosphatemia and at times acidosis, increase of the alpha-2-globulins, and generalized hyperaminoaciduria may be present.

Viral Respiratory Disease.—R. Sohier and co-workers (*Pédiatrie* 11:631, 1956) studied the frequency of acute infectious bronchitis and pneumonitis caused by viruses, with use of serologic tests for their identification. These tests included the use of cold agglutinins, Streptococcus MG agglutinins, and complement-fixation tests for the ornithosis group of viruses, A and B influenza virus, the adenoviruses, and Q fever. In 26 of 175 patients under 6 years with bronchopneumonia and 23 of 61 such children from 6 to 15 years, the infection was due to a virus. In patients with other diseases positive reactions were found only in 1.1% of those under 6 and 3.3% of those from 6 to 15 years of age. The positive reactions in many cases ruled out the diagnosis that had been made on admission.

Cutaneous Lesions Following BCG Vaccination.—R. Bastin and co-workers (*Pédiatrie* 11:681, 1956) report that in two children, aged 3 and 3½ years, a generalized exanthema developed over five weeks after BCG vaccination. These eruptions in the first child showed some similarity with polymorphous erythema, and in the second they had a morbilliform appearance. The first child had a leukocyte count of 50,000 per cubic millimeter, with a predominance of lymphocytes, and the second had a leukocyte count of 14,000, with an eosinophilia. The authors believe the eruptions to be due to primary infection with the BCG.

IRELAND

Tuberculosis.—As a result of improved treatment, the death rate from tuberculosis fell from 91 in 1949 to 34 in 1954 per 100,000 population. The number of new cases reported fell from 7,552 in 1949 to 6,266 in 1954. The health department recommends that young persons who show a negative reaction to the tuberculin test should be offered BCG vaccination, particularly if they live in rural districts and wish to move into the towns or go abroad. Many Irish immigrants to Great Britain contract tuberculosis. In the last five years, 1,300 returned from Great Britain to be treated for tuberculosis.

SWITZERLAND

Chlorpromazine and the Biliary Passages.—In 3 to 5% of the patients treated with chlorpromazine, jaundice appears. This complication is, to a certain extent, independent of the dose of the drug, but when it appears it is almost always in the third or fourth week of treatment. Its severity and duration are variable. The clinical findings are those of biliary obstruction, despite the absence of any obstruction. Errors of diagnosis are frequent and often lead to operative exploration, which shows the principal biliary passage to be empty and free of obstruction. Needle biopsy of the liver shows the biliary canaliculi to be gorged with thick, dark bile, with the formation of a kind of biliary thrombi, while the hepatic cells appear to be intact. The spontaneous course of the jaundice is toward a cure, either rapid or after weeks or months. The pathogenesis of chlorpromazine jaundice has not yet been elucidated. F. Besson (*Schweiz. med. Wchnschr.* 86: 1020, 1956) concluded that chlorpromazine provokes in most patients a prolongation of the time of closing of the sphincter of Oddi, an irregular outflow of the bile in slow spurts, and a delay in the emptying of the gallbladder. It is therefore a matter of the creation of a genuine biliary dyskinesia of a special type, similar to cystic dystonia or atony, which appears even after cholecystectomy. There is apparently a hypertonia of the sphincter of Oddi in relation to the weakness of the biliary flow. The biliary emptying is therefore almost routinely disturbed by chlorpromazine, but without evident effect in most patients. Clinically, this effect of chlorpromazine helps to explain the digestive sluggishness and stubborn constipation that occur so often in the course of treatment, and it is associated with the reduction of peristalsis and of the secretory activity of the gastrointestinal tract.

Diuretic Effects of Certain Polysaccharides.—It appears from experiments made by Desaulles and Meier (*Schweiz. med. Wchnschr.* 86: 1060, 1956) that in intact rats subjected to overloading with water or saline solution, certain polysaccharides possess the property of inducing general diuresis and an elimination of sodium increasing in intensity with the sodium concentration of the overload. Potassium excretion is not modified. These effects are met with only in normal animals. They can be antagonized by aldosterone and disappear in animals deprived of their adrenals. It seems unlikely that the mechanism of action of these substances is due to a direct effect favoring the elimination of salt and water and that the effect disappears as a result of the increase of renal elimination of sodium and the passage of increased quantities of extracellular sodium into the interior of the cell as a result of adrenalectomy. As these special types of action, observed after the injection of polysaccharides, bacterial among others, cannot be reproduced with the help of any known hypo-physial or adrenal factor, it must be concluded that these effects are either the result of a complex inhibition of one or more of these factors or that they are due to some unknown factor.

Radioactive Isotopes.—J. H. Muller (*Med. et hyg.* 14: 351, 1956) showed that it is possible to inject strong preparations of radioactive zinc in the form of quasi-colloidal suspensions of an insoluble sulfur into the abdominal cavity of patients affected by severe peritoneal carcinosis of ovarian origin. In 1949, Muller used radioactive gold (Au^{198}), in a colloidal form, for intraperitoneal and intrapleural injections for the same purpose. Its half-life of 2.69 days is ideal for applications of this kind. In 1950, the author extended the indication for peritoneal administration of Au^{198} colloid (with artificial hydroperitoneum of about 400 cc. in patients without ascites) to all patients with ovarian cancer whatever their degree of operability, as a supplement to standard postoperative radiotherapy. This combined radiological treatment has already been applied to about 130 patients, with results that are proving more and more clearly favorable. In fact, in this group of patients, all those with operable lesions (stage 1) have remained free from relapses and only 20% of the patients in stage 2 have had relapses. Intravenous injection of Au^{198} colloid results in a quasi-specific accumulation of radioactive particles at the level of the reticuloendothelial elements of the liver and the spleen. In one patient, Muller obtained, by means of such injections, the dramatic disappearance of an enormous lymphosarcomatous hepatosplenomegaly, and in various other patients a partial regression radiosensitive cancerous hepatic metastases.

UNITED KINGDOM

The *Minister's Annual* Report.—In his report on the National Health Service in England and Wales for 1955, the Minister of Health noted that the total cost of the service was 1,386 million dollars, an increase of 61.6 million dollars over the previous year. Of this sum, over 1,086 million dollars was met by the exchequer out of sums voted by Parliament. Only 100.8 million dollars was provided by contributions from the National Insurance Fund. This is equivalent to 12 cents out of each weekly total contribution for men, and it represents only a small fraction of the full weekly contributions paid by, or in respect of, insured persons. There is still a popular belief among the so-called working classes that their weekly contributions to the National Insurance Fund defray the entire cost of the National Health Service, which many of them use so freely. The minister's report shows that the contributions from the National Insurance Fund covered only 7% of the total gross cost of the service. Other sources of income were as follows: 19.6 million dollars paid by patients for dental treatment and dentures; 14 million dollars paid by patients for eyeglasses; and 13.8 million dollars paid by patients for drugs and appliances. This last sum is made up of the 14 cents that must be paid by each patient on every prescription dispensed for him under the service.

The hospital and specialist service costs 778.4 million dollars, which is just over 56% of the entire cost of the service. Hospital waiting lists, numbering only 453,000 persons, were the lowest recorded since the inauguration of the service. This decrease was most marked in the field of tuberculosis; the waiting list fell by 54% (from 3,017 to 1,387). In most areas, there are now no waiting lists for patients with tuberculosis. In spite of the fact that there was no increase in the number of hospital beds, the number of inpatients rose by 18,000, reaching a total of 3,600,000. The striking improvement in the tuberculosis situation is illustrated by comparing the 1955 figures with those of 1949. In the latter year, there were 19,908 deaths from tuberculosis, of which 17,559 were respiratory; 52,041 reported cases, of which 44,480 were respiratory; and a waiting list of 10,986. However, in 1955 there were only 6,492 deaths from tuberculosis, of which 5,837 were respiratory; 38,134 reported cases, of which 33,580 were respiratory; and a waiting list of 1,387. This vast improvement has made it possible to bring to an end the Swiss Sanatorium Scheme introduced in 1951 to relieve the strain on the sanatoriums in this country. Under that plan, 1,025 patients were sent to Switzerland for an average stay of six months at a total cost of just over 1.036 million dollars.

The number of full-time and part-time consultants rose by 2.1%, thus bringing the total to 6,650. These range from 801 in general medicine down to 44 in neurosurgery. The number of administrators fell by about the same percentage, but they still number over 28,000. The general medical service costs 147 million dollars. The number of principals in general practice under the service rose slightly, making a total of 18,832, of whom just under 7,000 practiced without an assistant or a partner. Of those in partnership, practically 10,000 were in partnerships of two or three, and only 289 were in partnerships of six or more. More than half of the assistants in general practice were 30 years of age or under, and nine were 76 years of age and over. Only 1,545 general practitioners attended refresher courses during the year. The pharmaceutical service cost 120.4 million dollars. During the year, 226,116,091 prescriptions were dispensed by pharmacists; this was 7,500,000 more than in the previous year. The average cost per prescription was 61 cents. The number of spectacles supplied was 4,500,000, and about 170,000 new and repaired hearing aids were supplied. The total number of persons now using hearing aids is 428,520.

Hospital Helicopter Landing Grounds.—Four hospitals in Cornwall are to have helicopter landing grounds in order to reduce the time taken in getting injured persons to the hospital by the R.A.F. Search and Rescue Service. This service, which was originally designed to rescue air crews that crashed in the sea, is now being used to an ever-increasing extent to rescue anyone in difficulty at sea or stranded on rocks. As Cornwall is one of the favorite playgrounds of England, with a coast line as noted for its dangers as for its beauty, every summer a number of persons lose or almost lose their lives in such accidents as falling down cliffs or getting stranded on rocks at high water. In the past, such persons, when rescued by helicopter, have first had to be taken to the helicopter base and then transferred to an ambulance to be taken to the hospital.

Vivisection.—The annual return of experiments on living animals, published by the Home Office, shows that 2,476,201 experiments were performed during 1955. The number of persons licensed to perform such experiments was 5,161, of whom 1,443 did not perform any during the year. About 87% of the experiments were performed without anesthetics. These consisted of inoculations, external applications, modifications of the animal's diet or environment, or the administration of a drug or toxin. In the study of cancer, 292 licensees performed 148,175 experiments. For public health purposes or for the diagnosis of disease, 180,303 experiments were made; these were usually simple inoculations. Over a million experiments were performed in the course of preparing and testing substances intended for use in the treatment of disease in man or animals.

Meals for Older Persons.—In September, 1955, a service of domiciliary meals for older persons was inaugurated in Rotherham. The first nine months of the service has been reported by Donaldson and Wales. (*M. Officer* 96:93, 1956). The plan is based on the assumption that every home has normally a certain amount of staple groceries and provisions and that if these were supplemented by the daily purchase of extra foodstuffs a full and varied diet could be provided for the patient. Of the 23 older persons selected for the program, all were over 80 years of age, lived alone, and had an income balance of less than $5.60 a week after the payment of rent and other weekly expenses. Twenty-one of the patients were housebound and 12 were bedfast. In each case the attendant at the home was given the sum of 88 cents a week with which to purchase supplementary food for five of the week's dinners. She was also given specimen menus as a general guide in achieving a balanced diet, but the patients were encouraged to suggest items for dinner so that their individual likes and dislikes could be respected. The general practitioners in charge of the patients were informed and consulted about the diet. At the end of the first nine months of the program, reports were obtained from the attending physicians; these showed a general improvement in the well-being of the patients. During the period, a total of 3,049 meals were served at a cost of $732. The two great advantages of the plan are that it provided for the personal predilections of the older persons and provided this by an existing service already operating in the home.

Postgraduate Courses for General Practitioners.—An account of a conference on postgraduate courses, organized by the College of General Practitioners, was published in *Research Newsletter* (no. 12) of the college. The Dean of University College Hospital London, reported that at his hospital they had been considering the appointment of general practitioners to various departments of the hospital and medical school. They were asking general practitioners to attend ward rounds and discuss with the students how, in their practice, patients might appear to them first. The dean agreed with the suggestion that a general practitioner should serve on the appointments committee, which selects students for the hospital. His hospital favored the suggestion that there should be a chair of general practice in each medical school.

Dr. J. G. McCrie, dean of the faculty of medicine at the University of Sheffield, reported that there were two representatives of the local faculty of the College of General Practitioners on the postgraduate committee of the university. This committee was responsible for arranging courses for general practitioners in and around Sheffield. In Sheffield it had been the custom for several years to provide for general practitioners, throughout the two winter terms, weekly ward rounds and clinical demonstrations. In response to 500 or 600 notices sent out, about 30 physicians usually attended. These were mostly the same persons each year. Evening lectures in pediatrics were popular. A general practitioner nominated by the local faculty of the college sat as a member of every selection committee. An arrangement was made by the professor of social medicine, in collaboration with the local division of the British Medical Association, for the attachment of final-year students to selected general practitioners for two weeks each. The program is voluntary, but few students fail to take advantage of it. The attachment was on a nonresidential basis, and Dr. McCrie considered that, if plans could be made that allowed for the student's residing in the physician's house, the program would be of much greater value. He wondered whether the setting up of a general practitioner unit attached to a university might not give a somewhat artificial view of general practice. No lectures were given in the university on general practice, but such questions as those about the structure of the National Health Service, statutory certificates, and medical ethics were included in the syllabus of certain classes. The local clergy have suggested that students should be instructed in cooperation with the clergy in the treatment of the sick.

Dr. Charles Newman, dean of the Postgraduate School of London, said that for general practitioners clinical evenings had proved successful originally but that the same people tended to come every time and that eventually attendance had fallen off. Lectures had not been satisfactory, as general practitioners did not find them clinical enough. Discussion panels were useful as an occasional activity, but they were not flexible enough to form a regular weekly feature. Lecture-demonstrations had not proved successful nor had general ward rounds. In the end the best technique had proved to be to give special demonstrations in the wards: teaching over the bed and contrasting the condition of one patient, such as a patient with asthma with consequent bronchitis, with that of another patient, such as a patient with bronchitis showing bronchial spasm.

Dr. E. C. Warner, the dean of Charing Cross Hospital, described the plan in operation there. Students in the final six months of their clinical period are sent out to selected general practitioners for a course of instruction in general practice. A very important feature is that, in almost every case, the student lives with the physician during this time. It was found that the ideal period was three weeks. While the students are with the general practitioners, they examine as many patients as possible, both in the office and in the patients' homes. The patients rarely objected to the presence of the student. Although at first the students were averse to the program, they have become enthusiastic about it, and some have voluntarily arranged to stay with the physician for a fourth week. The cost of board and lodging is covered in part by the student and in part by the medical school.

WORLD HEALTH ORGANIZATION

Whooping Cough.—Although whooping cough is still often considered to be of relatively little importance, it kills more babies during the first year of life than all the other common diseases of childhood combined (Annual Epidemiological and Vital Statistics Report, vol. 9, no. 6, Geneva, World Health Organization, 1956). Deaths from whooping cough have shown a marked and continuous drop in the past 50 years, but the decrease has been much less than that observed in the death rates for other communicable diseases such as diphtheria, scarlet fever, and measles. Moreover, the drop in mortality began before the discovery of effective means of protection, and this fact has not been satisfactorily explained. Despite fewer deaths, the number of cases has not diminished and the disease affects as many people as ever. Whooping cough also appears to be unique among the infectious diseases, in that it usually strikes and kills more girls than boys. Recently there has been a rapid rise in reported cases of whooping cough from certain countries and territories, but this could be attributed to better medical reporting rather than to a real increase in the prevalence of the disease. The statistics collected indicate that whooping cough affects a greater proportion of young children in southern (Egypt, Portugal, Italy) than in northern countries.

Accident Prevention.—The World Health Organization regional committee for Europe reports that, in Great Britain, 45 people on an average lose their lives every day as the result of accidents, 16 in some form of travel (14 on the road, 1 on the railways, and 1 in air or water transport), 5 at some place of work (2 in factories, 1 in coal mines, and 2 in farms, quarries, and other places of work), and 24 in and around the home (17 inside the home and 7 in ordinary pursuits around the home). In the Netherlands also, traffic accidents are not the most frequent cause of accidental death. In Italy, the pattern is similar. The average daily accident toll is 44 killed (7 at work, 20 in travel, and 17 at home and elsewhere). In Finland in 1955, 36% of all deaths in the age group 1 to 14 years were due to accidents. About half of these were drownings (unlike the pattern in Great Britain, where drownings are rare). In Germany, accidents in the home account for more than 30% of all fatal accidents. In Yugoslavia, among hospital patients, almost 20% of the deaths result from accidents. Rapid industrialization in that country has led to a serious increase in accidents.

In Norway, efforts are being made to reduce the number of drownings in open disused wells, and legislation that will make owners responsible has been drafted. In France during the last 15 years or so, burns and scalds have become less frequent but falls out of windows and from high structures have become more frequent. A new and growing hazard in the home is poisoning. On the one hand, there are insecticides and corrosive liquids that are kept *in many* homes, particularly on farms; on the other, there are dangerous medicines that the manufacturers have tried all too successfully to make attractive with bright wrappings, pretty colors, and sugar coating on the pills. In Iceland, drowning has been decreasing as a cause of death. Swimming lessons are compulsory, and by use of the Icelandic hot springs many bathing pools have been made in which even the smaller children are happy to test their courage and skill. Traffic accidents are being reduced in Austria by getting children to take part in controlling the traffic. In that country, children are also being brought into factories and other places where danger is present. An account was given of a large block of flats where the automatic elevator was used by children but did not cause any accidents. A committee of children was responsible for keeping it clean and in good running order.

The following points were stressed: 1. Information about fatal accidents is much more complete and accurate than the records of injuries that do not result in death. Accidental deaths are relatively frequent in children under 5 years of age and in persons over 60. 2. Fatal accidents have become relatively more frequent in recent years because of the decrease in deaths from infectious diseases. There is also an absolute increase due to hazards associated with increasing mechanization. 3. The available statistics deal almost exclusively with fatal accidents, but *the nonfatal accidents, which are perhaps 100 times as common*, give rise to a great amount of suffering, disability, and economic loss. 4. There is an urgent need for more intensive studies of nonfatal accidents, as the evidence suggests that their pattern differs from that of fatal accidents. For example, fatal injuries in the home tend to cluster around persons in the extremes of life, but the nonfatal accidents affect principally the housewife and the adolescent children. 5. Special attention should be given to preventive measures. Houses and household equipment should be designed for safety, especially electrical appliances and sources of heat. Children and elderly people should be protected from dangerous drugs, corrosive liquids, and other hazards. The committee laid great stress on education as the greatest single measure in the prevention of accidents. This includes the careful training of children at home and in school and especially giving them a sense of responsibility for their own safety. It comprises also the training of teachers and parents through films, radio, television, posters, and booklets.

Dr. Sutter Resigns.—Dr. Victor A. Sutter, assistant director-general in charge of advisory services in the World Health Organization, in Geneva, has resigned his position in order to accept an appointment as Minister of Public Health and Social Assistance in his own country, El Salvador. Dr. Sutter, a member of the WHO staff since 1950, studied at the National University of San Salvador and at Johns Hopkins University in Baltimore.

Regional Director for Europe.—The regional committee for Europe elected Dr. P. J. J. van de Calseyde as its nominee for the post of World Health Organization regional director for Europe. The post became vacant as the result of Dr. Begg's death earlier this year. Dr. Van de Calseyde's name will be sent for endorsement to the WHO executive board in January. At present he is director-general of health at the Ministry of Health, Brussels, Belgium.

Resistance of Insects to Insecticides.—Leadership in the stimulation and coordination of research throughout the world on the problem of resistance of insects to insecticides should be assumed by the World Health Organization, according to a group of experts. Great alarm has been caused by the appearance of resistance to such insecticides as chlorophenothane (DDT) among certain species of insects. In the housefly, resistance to insecticides is becoming universal. It is also of frequent occurrence in the body louse and exists locally in several species of mosquitoes. WHO should coordinate the different lines of research on the problem of resistance already being undertaken in laboratories scattered throughout the world; stimulate further research, particularly concerning the physiology, biochemistry, and genetics of the insects concerned; assure the publication and exchange of information and research results; and facilitate the procurement of qualified personnel and funds for research. Standard techniques should be adopted or developed for detecting and measuring resistance, and WHO should circulate information concerning new insecticides as it becomes available.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Rapid Diagnosis of Human Influenza Infection from Nasal Smears by Means of Fluorescein-Labeled Antibody. Ch'ien Liu. Proc. Soc. Exper. Biol. & Med. 92:883-887 (Aug.-Sept.) 1956 [Utica, N.Y.].

In the study of influenzal infection in ferrets by means of fluorescein-labeled antibody, it was possible to make a rapid diagnosis of influenzal infection during the acute stage of illness by detecting specific viral antigen in the desquamated nasal epithelial cells and macrophages in the nasal smears. This paper reports the application of this method to influenzal infection in humans. The method was applied to 20 patients during an outbreak of influenza A-prime infections, to 44 during an outbreak of influenza B, and to 23 patients with various acute febrile or respiratory illnesses. With a rise of fourfold or greater in titer of hemagglutination-inhibition (HI) antibody during convalescence or else the recovery of virus from human nasal washings used as diagnostic criteria for influenzal infection, the use of fluorescent antibody had an accuracy of 71% in an influenza A-prime and 38% in an influenza B epidemic. One false-positive diagnosis was encountered among 23 noninfluenzal infections. The use of labeled antibody on smears of nasal washings is less sensitive than the HI test, but a positive diagnosis could be made on the day the specimens were collected, while the HI test requires a delay of 10 to 14 days for collection of convalescent serum.

Hypertensive Pulmonary Vascular Disease. D. Heath and W. Whitaker. Circulation 14:323-343 (Sept.) 1956 [New York].

The authors describe six cases of severe pulmonary hypertension in four women between the ages of 21 and 58, one 24-year-old man, and one 12-year-old girl. The condition was complicated by a ventricular septal defect, Eisenmenger's complex, patent ductus arteriosus, atrial septal defect, and mitral stenosis, respectively, in the five adult patients; the child had idiopathic pulmonary hypertension. The clinical picture was dominated by symptoms and signs characteristic of pulmonary hypertension, which often masked underlying cardiac anomalies. Symptoms of severe pulmonary hypertension were breathlessness on exertion, frequent cough and colds, chest pain of anginal type, blueness of the lips and nails, and abdominal distention and swelling of the ankles due to congestive cardiac failure. Hemoptysis, hoarseness, jaundice, syncopal attacks, and palpitation occurred less commonly. Signs associated with pulmonary hypertension were giant "a" waves in the jugular venous pulse, a parasternal heave, a systolic lift over the right ventricular outflow tract, a palpable second sound in the pulmonary area that was loud and closely split on auscultation, a Graham Steell murmur, and a pulmonary systolic click. In addition, central and peripheral cyanosis, clubbing of the fingers, jaundice, signs of congestive cardiac failure, and cardiac murmurs occurred. The electrocardiogram usually showed clockwise rotation of the heart and the ventricular pattern of right ventricular hypertrophy. On radiological examination there was evidence of right ventricular hypertrophy, increased prominence of the pulmonary artery and its main branches, and decreased peripheral pulmonary vascular markings. Angiocardiography revealed a dilated pulmonary artery and a coppicing effect in the small branches of the pulmonary vascular tree. The flow of dye through these dilated vessels was abnormally slow. It allowed abnormal flows to be visualized and previously unrecognized cardiac defects to be demonstrated. Cardiac catheterization showed pulmonary artery blood pressures approaching or exceeding systemic pressures and occasionally revealed intrinsic cardiac defects.

Five of the patients died and autopsy was performed in all of these. The definitive pathological changes in the pulmonary vasculature were a distinct muscular media with two elastic membranes in the pulmonary arteriole and medial hypertrophy in the muscular pulmonary artery. Frequently in these vessels there was abnormal proliferation of intimal fibrous tissue with partial or complete occlusion of the lumen, adventitial fibrosis, and medial necrosis. Occasionally there was aneurysmal dilatation of thin-walled branches of the muscular pulmonary arteries.

Patients with pulmonary artery blood pressures chronically elevated to levels approaching or exceeding systemic pressures demonstrate a distinct clinicopathological entity for which the term hypertensive pulmonary vascular disease is proposed.

Peroral Maintenance Treatment of Pernicious Anemia with Vitamin B_{12} and Intrinsic Factor. H. Olsen. Ugesk. læger 118:895-897 (Aug. 2) 1956 (In Danish) [Copenhagen, Denmark].

Twelve patients with pernicious anemia who were treated from the start with vitamin B_{12} and intrinsic factor by mouth and reacted well to the treatment were examined after from 10 to 34 months of treatment. The blood status was satisfactory in all cases, and the neurological symptoms present at the beginning of treatment had disappeared. No new neurological symptoms attributable to the hematological disease had developed.

Constrictive Pericarditis: A Review and Long-Term Follow-Up of 78 Cases. J. C. Dalton, R. J. Pearson Jr. and P. D. White. Ann. Int. Med. 45:445-458 (Sept.) 1956 [Lancaster, Pa.].

Dalton and associates reviewed the clinical aspects of 78 patients with constrictive pericarditis, of whom 59 were males and 19 females. Sixty-five of the patients were operated on, and 42 of these are still living. Six have been followed for over 20 years, 10 for over 10 years, and 11 for over 5 years. All of the patients followed over 20 years are living normal, unrestricted lives. There were several operative deaths among 61 patients who underwent 71 operations. Of the seven patients who were operated on more than once, two died. Excellent results were obtained by operation in 32 of 64 patients and fair results in 13 (14 operations); no improvement resulted in 5 of the patients. The two groups of patients who obtained excellent and fair results were compared with regard to their preoperative status. The only positive correlation was that 29 of the 32 patients in the "excellent result" group were in sinus rhythm preoperatively, while three had atrial fibrillation. Of the 13 patients classified as having "fair results," only five were in sinus rhythm preoperatively, while eight had either atrial flutter or fibrillation as their basic rhythm. It is interesting that all six patients who had been followed for over 20 years and who are considered as having excellent results had normal rhythm preoperatively and at last examination in 1955.

Duration of symptoms, heart size, and calcification of the pericardium were compared in the two groups and showed no significant differences. Dyspnea on exertion, ankle edema, and abdominal swelling, in that order, are the most frequent complaints at the onset and as the constrictive pericarditis progresses. Among the physical findings, hepatomegaly and distention of the neck veins remain the most common. A systolic blood pressure above 130 mm. Hg was found in only one patient preoperatively, whereas wide pulse pressures were not rare (greater than 50 mm. Hg in 9% of cases). Systolic blood pressures commonly rose postoperatively, but no patient became seriously hypertensive. Cardiac enlargement was present in one-half of the patients. Cardiac pulsations were diminished in four-fifths but were fluoroscopically normal in the other fifth of the patients. Abnormal electrocardiograms were present in every pa-

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The place of publication of the periodicals appears in brackets preceding each abstract.

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tient; the T waves were abnormal in 100% and the P waves in 72% of those with normal rhythm. Atrial arrhythmias were common, having been found in 34 of the 78 patients; fibrillation was identified in 27, being constant in 19, while flutter occurred in 3, in 2 of whom it changed to fibrillation. Calcification was noted in the pericardium in 60% of the patients.

Serum Hepatitis Following Dental Procedures: A Presentation of 15 Cases, Including Three Fatalities. F. E. Foley and R. N. Gutheim. Ann. Int. Med. 45:369-380 (Sept.) 1956 [Lancaster, Pa.].

Various skin-penetrating procedures have been known to be followed by serum hepatitis. The members of the house staff of the Rochester General Hospital, Rochester, N.Y., first became aware of the appearance of hepatitis after dental procedures in 1952. The charts of all patients treated at that hospital for infectious or serum hepatitis between June, 1953, and June, 1955, were studied. Of 57 patients with viral hepatitis, 7 contracted serum hepatitis after blood or plasma transfusions. The remaining 50 patients ordinarily would have been considered as having infectious hepatitis. Fifteen of these patients, however, gave a history of a dental injection during the preceding one to six months and are referred to as the dental serum hepatitis group. These dental injections consisted of the injection of procaine during the process of extracting teeth in 13 patients and the filling of teeth in 2 patients. Two of the 15 patients had received penicillin injections at the same time as the procaine injections. The ages of the patients ranged from 18 to 71 years. The onset of illness in 14 patients was insidious in nature. The remaining patient had a rather acute onset. Malaise, fatigue, and anorexia, alone or in various combinations, were the first symptoms in all but three of the patients. Nausea and abdominal pains were next in frequency. Laboratory data obtained in the 15 patients were characteristic of viral hepatitis. Three fatalities occurred in this group. Heat sterilization of needles, syringes, and instruments is essential to prevent the spread of serum hepatitis. The danger of the use of multiple injection bottles is emphasized.

Lupus Erythematosus, Discoid and Systemic: One Disease. M. F. Allende. Postgrad. Med. 20:254-259 (Sept.) 1956 [Minneapolis, Minn.].

Allende presents clinical, histopathological, experimental, and therapeutic evidence to support the concept that chronic discoid lupus erythematosus and systemic lupus erythematosus are merely variants of a single disease. Chronic discoid lupus erythematosus should be considered as the mildest form of systemic lupus erythematosus. Patients with chronic discoid lupus erythematosus should be warned about the dangers of actinic radiation, of the use of potentially toxic drugs, of minor infections, and of the indiscriminate removal of so-called foci of infection. They should be checked at regular intervals with physical examinations supplemented by determination of the sedimentation rate of the erythrocytes, by complete blood counts, and by urinalysis. These measures should be supplemented by a search for the L. E. phenomenon if imminent dissemination is suspected.

Agammaglobulinemia. S. Aarseth. Tidsskr. norske lægefor. 76: 505-507 (Aug. 1) 1956 (In Norwegian) [Oslo, Norway].

A case of primary idiopathic agammaglobulinemia in a man aged 41 is the first in an adult observed in Norway. The patient manifested, from early childhood on, a tendency to infections of the respiratory tract. He had the usual childhood diseases, recurrent bilateral purulent otitis, and from the age of 16 on a purulent sinusitis. He has had pneumonia at least 14 times. There are bronchiectases with type 3 pneumococci. A purulent meningococcus meningitis in June, 1955, yielded to intensive penicillin and sulfonamide treatment. Pneumonia shortly thereafter was successfully treated with aureomycin. In December, 1955, he had meningitis due to type 3 pneumococcus; again treatment with massive doses of penicillin and sulfonamide was effective. At this time severe diabetes of the insulin-deficient type was discovered. Agammaglobulinemia was suspected because of the patient's unusual tendency to infections. Electrophoretic examination showed the patient to be practically without gamma globulin. In agammaglobulinemia the respiratory tract is primarily exposed to infection. Bronchiectases belong in the picture. No special tendency to tuberculosis is seen. Generalized vaccinia with a fatal outcome has been noted in agammaglobulinemia, and children with this anomaly should not be vaccinated against smallpox. Prophylactically, patients with the disease can be protected against infection by the administration of gamma globulin in doses of 100 mg. per kilogram of body weight monthly; an alternative is application of an antibiotic—slow-acting penicillin—or a sulfonamide. An accumulation of infections in a patient calls for paper electrophoretic examination of the serum. It is the simplest diagnostic method for clinical use. In the case in question the combination of agammaglobulinemia, severe diabetes, and extensive bronchiectases infected with pneumococci make the long-range prognosis doubtful.

SURGERY

Adrenalectomy for Intracranial Metastases From Carcinoma of the Breast. A. Clain and A. H. Hunt. Brit. M. J. 2:627-629 (Sept. 15) 1956 [London, England].

At the Royal Marsden Hospital over 90 adrenalectomies had been performed up to the end of 1955. In only two patients were cerebral metastases clinically evident. The first patient, a 37-year-old woman, had been subjected to radical mastectomy for anaplastic carcinoma of the left breast in August, 1948. Carcinoma of the whole of the right breast, with peau d'orange and a retracted nipple and extensive involvement of the axillary nodes was found in January, 1951. Bilateral oophorectomy was performed and a course of x-ray therapy given to the right breast and glandular areas. The local progress of the disease was arrested. Thereafter the condition remained unchanged until November, 1954. At that time personality changes were evident. Radiograms of the skull showed expansion and destruction of the pituitary fossa, presumably from erosion by growth. The left lung contained multiple metastases. A large quantity of ascitic fluid was present. She was given daily doses of 1,000 mg. of testosterone propylpropionate for three days and 50 mg. of cortisone for five days. Her diabetes insipidus was treated with pitressin. On Nov. 23, it was felt that she was fit for surgery. Both adrenal glands were removed at one operation. She made a slow but steady recovery. Her mental symptoms cleared up and the diabetes insipidus gradually improved, though she still required small doses of pitressin. She has remained reasonably well up to the time of this report, 22 months after operation.

The second patient, a 40-year-old woman, also had cerebral metastases after a right radical mastectomy for anaplastic carcinoma. Her neurological state likewise recovered rapidly after removal of the right adrenal, the left adrenal having been removed at the time of bilateral oophorectomy seven days earlier. The authors conclude that bilateral gonadectomy and adrenalectomy is at present the only treatment of value for patients with intracranial metastases from cancer of the breast. It should be attempted when possible, because these patients are otherwise doomed. Hypophysectomy, whatever its place may be in the treatment of the other manifestations of metastatic breast cancer, has no place in the palliation of cerebral metastases.

Observations of Human Adrenal Cortical Deficiency with Special Reference to Replacement Therapy with Cortisone. A. G. Hills, H. A. Zintel and D. W. Parsons. Am. J. Med. 21:358-379 (Sept.) 1956 [New York].

Adrenalectomies have been performed in the University of Pennsylvania Hospitals as an experimental therapeutic approach to severe hypertensive disease. The studies presented deal particularly with two aspects, namely, (1) whether surgically produced primary adrenal deficiency in man differs in kind or in degree from spontaneously occurring Addison's disease, and (2) to what extent cortisone (with or without supplementation with desoxycorticosterone) falls short of furnishing entirely satisfactory maintenance therapy for adrenal-deficient man. The results of a five-year study of 44 patients subjected to adrenalectomy are presented together with observations of 9 patients in whom Addison's disease occurred spontaneously. Cortisone, often supplemented by a small quantity of desoxycorticosterone, was given as replacement therapy. Steroid therapy is indispensable for the survival of persons who have been subjected to total adrenalectomy, but some patients with Addison's disease and some subtotally adrenalectomized persons can survive and maintain well-being without it. Such patients apparently enjoy a nearly normal basal rate of adrenal cortical secretion. The survival value of this secretion can be estimated as corresponding to the amount of steroid that will just maintain a totally adrenalectomized man in good general health (that is, assuming adequate salt intake, about 30 mg. of orally administered cortisone acetate daily, supplemented by 1 mg. of desoxycorticosterone acetate given by the buccal route.

Few patients with Addison's disease are totally destitute of endogenous adrenal cortical secretion. Approximately 5% of the total amount of adrenal cortical tissue normally present will produce enough secretion to sustain life under ordinary circumstances. This quantity of surviving tissue has, however, practically no capacity to increase its basal hormone output, and a patient without ample cortical reserve is imperiled by any stress unless exogenous hormone can then be supplied. Cortisone can maintain the life of totally adrenal-deficient persons indefinitely and can restore strength and well-being, but it does not provide a balanced replacement for the missing adrenal cortical secretion, of which cortisone and hydrocortisone are only partial constituents. There is no truly "physiological" quantity of cortisone, that is, there is no dose of cortisone that, on long-term administration to adrenal-deficient patients with or without a small supplement of desoxycorticosterone, will not be accompanied by certain signs of hypoadrenalism or certain manifestations of hypercortisonism or both. The signs of hypoadrenalism commonly encountered in such patients are melanosis, impairment of water diuresis, unresponsiveness to hypoglycemia, and sometimes salt waste, azotemia, and hyperkalemia. The signs of hypercortisonism are polyphagia, weight gain, and impairment of glucose tolerance. No fundamental distinction can be drawn between spontaneous and iatrogenic primary adrenal cortical deficiency. The incidence of melanosis has been strikingly lower in patients rendered adrenal-deficient by surgery than in persons with spontaneous Addison's disease, but this difference can probably be ascribed to the provision of cortisone to the former group from the time of origin of the adrenal-deficient state. However, although cortisone has antipigmentary properties in adrenal-deficient persons, the adrenal cortex must contain antipigmentary factors other than cortisone and hydrocortisone. Clinically detectable regeneration of adrenal cortical tissue occurred only once in a series of 27 patients subjected to subtotal adrenal resection.

On the So-Called Abscess Cancer of the Lungs. L. Morelli and L. Di Domizio. Arch. ital. chir. 81:181-201 (No. 3) 1956 (In Italian) [Bologna, Italy].

Cavitary cancer of the lung, or abscess cancer, is a type of bronchogenic carcinoma; it is characterized by a cavity of recent formation that contains purulent necrotic material. The authors observed 12 such cases of cancer, 8 primary and 4 secondary. Among the eight primary cases, histological examination demonstrated small-cell carcinoma in six patients and polymorphous carcinoma in one. Of the four secondary forms, three belonged to the polymorphous type and one to the small-cell type. Radiological examination was useful in the general diagnosis of cavitary suppuration, but it was not so useful in the diagnosis of carcinoma. Bronchoscopy was performed in all cases. Biopsy of metastatic supraclavicular lymph nodes confirmed the clinical diagnosis. Six patients underwent surgery: one explorative thoracotomy, three pneumectomy, one lobectomy, and one pneumotomy. Ten patients were over 45 years of age, one was 43, and another was 41; there were 11 men and one woman. The symptoms, which were almost the same in all cases, included cough with little expectoration always tinged with blood, fever, and dyspnea. In some patients symptoms had been present for 12 months and in one case for two years. Surgical intervention is necessary if the combined therapy for pulmonary suppuration gives no result in from four to eight weeks, especially if the patient is over 45 years of age.

The Aggressive Treatment of Metastases. E. Wilson. M. J. Australia. 2:292-297 (Aug. 25) 1956 [Sydney, Australia].

The author believes that, while the future treatment of metastases lies more with hormonal and other methods, surgical treatment holds the first place at present. Not only is surgery advisable after metastases have been detected clinically, but there is also a place for elective reexploration to search for and to deal with metastases before they are otherwise detectable. In the absence of metastases at the primary operation, elective reexploration of the abdomen should be considered within six months in patients with carcinoma of the colon, ovary, liver, pancreas, and rectum, and slightly earlier in those with carcinoma of the stomach. In all cases in which a second operation has already been required for the eradication of a metastatic mass and where there is no evidence of any other metastasis, an elective reexploration should be strongly recommended. Supraradical surgery has a place in the early stages of certain cancers rather than in the subterminal stages of the disease. However, supraradical surgery is occasionally indicated even for palliation. A case is described in which symptoms of hepatic insufficiency were temporarily relieved by litigation of the branch of the hepatic artery to that particular lobe destroyed by the metastases. The relief was probably due to the resulting increased blood supply of the lobe that contained most of the functioning hepatic tissue.

More study should be given to (1) the effects on cancer cells of substances that stimulate the growth or metabolism of normal cells, (2) the reasons why some malignant growths do not metastasize, (3) the use in "hormone-dependent" cancers of hormone therapy and of hormone exclusion operations, especially hypophysectomy produced by both surgical and medical means, (4) the place of elective reexploration in the management of intra-abdominal and other cancers, and (5) the positions of metastases in specimens removed from patients apparently cured by surgery. Such study would provide a basis for determining the extent of the operations to be employed for various cancers.

Scalene Node Biopsy: An Analysis of 42 Cases. W. W. Yang. California Med. 85:165-166 (Sept.) 1956 [San Francisco].

Scalene node biopsy was done in 42 patients with previously undiagnosed intrathoracic lesions. The basis of the scalene node or fat-pad biopsy is that lymph nodes anterior to the scalenus anticus muscle are connected with the mediastinal nodes. Thus intrathoracic disease involving the mediastinal nodes may often be reflected in the scalene nodes. The same is true of systemic disease directly involving the mediastinal nodes. The simple scalene node biopsy hence is a biopsy of the mediastinal nodes without the necessity of entering the thorax. A definite histological diagnosis was obtained in 25 of the 42 patients. Carcinoma of the lung was detected in nine patients, metastatic tumor to the lung in eight, pulmonary tuberculosis in three, lymphoma in three, anthracosis in one, and sarcoidosis in one. Scalene node biopsy is especially useful in patients with bronchogenic carcinoma. In this disease the value of this biopsy is twofold: 1. A diagnosis may often be obtained without thoracotomy. 2. In such cases, and also in those in which the diagnosis has been made by other means, the procedure is of value in determining the prognosis. When a scalene node biopsy is positive for cancer, there has been considerable extension of the carcinoma; operability is then questionable. Complications are rare in scalene node biopsy. Hemorrhage due to injury to the jugular vein occurred in one of the patients in this series, but it was readily controlled. Scalene node biopsy is a valuable diagnostic procedure.

NEUROLOGY & PSYCHIATRY

Subarachnoid Haemorrhage Due to Intracranial Aneurysms: Results of Treatment of 249 Varified Cases. W. McKissock and L. Walsh. Brit. M. J. 2:559-565 (Sept. 8) 1956 [London, England].

A survey of 461 patients with subarachnoid hemorrhage admitted to St. George's Hospital in London up to March 31, 1954, revealed that in 249 the hemorrhages were caused by an aneurysm. The data on the 249 patients with proved intracranial aneurysm associated with subarachnoid hemorrhage are analyzed in relation to the severity of the effects of the hemorrhage and the site of the aneurysms. The results of various types of surgical treatment are compared with those of medical treatment. The frequency of associated intracerebral, intraventricular, and subdural hemorrhage is given. The frequency and time of occurrence of repeated hemorrhage is considered, and the operation of carotid ligation is discussed. Very early investigation and treatment of patients with a bleeding aneurysm seems advisable because a lower mortality has been shown to occur in cases handled in such a manner than is to be expected from the natural course of the disease. In medically treated patients with anterior communicating or middle cerebral aneurysms the natural death rate is over 90%. If even a few patients can be restored to reasonable health by surgical measures, the operative mortality rate should surely be assessed against the natural death rate of 90%, and so even a 50% operative mortality rate would be acceptable.

An Investigation of Neurosurgical Alleviation of Parkinsonism, Chorea, Athetosis and Dystonia. I. S. Cooper. Ann. Int. Med. 45: 381-392 (Sept.) 1956 [Lancaster, Pa.].

Cooper summarizes the current status of the neurosurgical treatment of several hyperkinetic disorders, particularly Parkinsonism. He reviews observations made in the course of 200 operations, 180 of which were performed for Parkinsonism. The remaining 20 were performed in patients with various other hyperkinetic disorders, which could be grouped as chorea, choreoathetosis, tension-athetosis, and dystonia musculorum deformans. Fifty-five of these operations consisted of surgical occlusion of the anterior choroidal artery; the other 145 were chemopallidectomies. The operation of anterior choroidal artery occlusion is best suited for young patients with postencephalitis Parkinsonism of long duration. It has the disadvantage of being dependent upon the vagaries of the anterior choroidal artery, but it may produce great benefit in a reasonable percentage of patients. Therefore, in selected instances, the risks of this procedure are justified.

Chemopallidectomy is of potential value in all types of Parkinsonism. Its technique has the advantage of being accurate, straightforward, and simple to execute. In fact, its simplicity could easily lead to abuse and incorrect usage. Chemopallidectomy provides an opportunity to select the correct subcortical site for destruction by the performance of an intracerebral procaine injection before the infliction of a permanently destructive lesion. Thus, the effect in a given patient can be predicted with a reasonable degree of accuracy. The risk of this operation is low, the mortality rate being less than 3%. The possibilities of lasting benefit are good—at least 70% at the present time. There is at present no cure for Parkinsonism. There is, however, the possibility of useful alleviation of many of its symptoms by neurosurgery. There is as much, if not more, justification for the neurosurgical treatment of Parkinsonism as there is for the neurosurgical treatment of intractable pain or of focal epilepsy. The approaches described are new, but their cautious and expert use will not only give relief to patients but will also increase the knowledge needed to advance the therapy of hyperkinetic diseases.

Prenatal Obstruction of the Fourth Ventricle. D. D. Matson. Am. J. Roentgenol. 76:499-506 (Sept.) 1956 [Springfield, Ill.].

Successful treatment of hydrocephalus depends upon an accurate knowledge of the location and type of obstruction to normal cerebrospinal fluid movement. Matson describes one type of hydrocephalus, namely, that due to prenatal obstruction of the foramens of Magendie and Luschka, in which the roentgenographic findings are pathognomonic. Obstruction of the normal foramens between the fourth ventricle and the surface subarachnoid pathways dating from early embryonic life falls into the category of congenital anomalies in which the earliest possible recognition is not only desirable but of the greatest importance in obtaining a satisfactory surgical result. This obstruction of the fourth ventricle has been observed at the author's clinic during the last four years in eight infants under six months of age.

Congenital obstruction of the fourth ventricle foramen should be suspected from the clinical appearance of the patient in the first months of life. The diagnosis can always be confirmed preoperatively by roentgenographic examination, including plain skull roentgenograms, ventricular air studies, and dural sinus venography. In this condition a huge cyst fills a much enlarged posterior fossa and projects downward into the cervical spinal canal as well as upward through the incisura of the tentorium. The tentorium fails to descend and is attached high on the parietal bones. There is obstructive internal hydrocephalus, which in some patients may be relieved completely by suboccipital craniectomy with excision of the cyst wall; in others it is converted to a communicating type of hydrocephalus, which must subsequently be treated by creation of a peritoneal or ureteral shunt. No surgical death occurred in the eight infants operated on at the author's clinic, but one patient died two months after operation with progressive communicating hydrocephalus complicated by convulsive seizures. Three of the remaining patients are doing well with no further treatment than wide excision of the cyst wall. In the other four patients excision of the posterior fossa cyst has had to be supplemented by spinal fluid shunting procedures to maintain normal intracranial pressure. The earliest possible recognition and definitive treatment of this lesion offers the best chance for a satisfactory result—and by satisfactory result is meant not survival, but opportunity for normal mental and motor development of the child.

Hemorrhagic Diathesis in Poliomyelitis. T. Bennike and L. C. Grandjean. Acta med. scandinav. 155:225-236 (No. 3) 1956 (In English) [Stockholm, Sweden].

Fifty-one (15%) of 349 severely paralyzed patients with poliomyelitis who were admitted to the Blegdams Hospital in Copenhagen, Denmark, during the 1952-1953 epidemic of poliomyelitis had a clinically manifest hemorrhagic diathesis in the form of bleeding into the skin, bleeding from mucous membranes and internal organs, and bleeding after tracheobronchial aspiration. The bleeding tendency was most pronounced in the most severely affected patients and occurred particularly within the first two weeks of the illness. Tracheobronchial hemorrhage predominated, but hematuria was also observed frequently. A systematic examination of 115 patients with poliomyelitis with varying degrees of paralysis revealed that 80% of the patients, irrespective of the presence or absence of a bleeding tendency, had abnormal capillary fragility. This persisted with little change for at least four or five months after the onset of the disease. These observations suggest that the hemorrhages were, at least in part, of vascular origin, since abnormal capillary fragility was the only regularly occurring defect in the hemostatic mechanism. The slow subsidence of the observed changes favors a neurogenic causation. An interplay may be considered between the reduced capillary resistance and one or more unknown factors, possibly resulting from the unphysiological state of many patients during the acute phase of the disease. The results of experiments in animals carried out by other workers suggest that the poliomyelitis infection may be associated with the occurrence of autoantibodies, possibly caused by the destruction of tissue resulting from the infection, which may have a harmful effect on the capillary wall.

PEDIATRICS

Congenital Nonhemolytic Jaundice with Disease of the Central Nervous System. I. M. Rosenthal, H. J. Zimmerman and N. Hardy. Pediatrics 18:378-386 (Sept.) 1956 [Springfield, Ill.].

The authors describe a case of persistent severe jaundice and progressive neurological disease in a 5-year-old boy. The neurological symptoms did not appear until he was 3 years old, although the jaundice was first noted when he was 2 days old. The condition was either the same as or closely related to the "congenital nonhemolytic jaundice with kernicterus," recently described by Crigler and Najjar in eight members of a single large family, although the patient was not a blood relative of this family. The jaundice observed in this condition is the result of the reduced capacity of the liver cells to metabolize and excrete bilirubin, but the pathophysiological mechanism remains obscure. The neurological syndrome consisted of staggering gait, slow and scanning speech, and an intention tremor. An electroencephalogram revealed irregular high voltage, 5 to 8 per second activity with some 3 to 5 per second activity in all areas. Atypical irregular sleep frequencies with a few suggestive discharges were present in the temporal areas. The neurological syndrome is believed to be the result of bilirubin encephalopathy. The authors prefer to use this term to signify damage to the central nervous system resulting from the toxic effects of bilirubin on the brain, and they believe the term "kernicterus" should be restricted to the pathological findings of pigmentation of the basal nuclei.

At laparotomy the patient's liver and gallbladder appeared normal, and the extrahepatic biliary system was patent. Biopsy of the liver was performed, and sections showed that the parenchymal cells were essentially normal. There was some vacuolization of many nuclei. No bile pigment was detected within the cells. In the portal areas, around the central veins, and occasionally between the liver cords were small foci of inflammatory cells. The patient made a good recovery from the operation. He has become able to walk a short distance unaided, but with a markedly ataxic gait. However, he is no longer able to feed himself. The course of this patient indicates that development of bilirubin encephalopathy is not necessarily confined to infancy. It can, apparently, occur in young children, and probably in older children and adults, if the concentrations of indirect-reacting bilirubin in the serum are sufficiently high for a prolonged period.

Transient Dysproteinemia in Infants, a New Syndrome: I. Clinical Studies. R. A. Ulstrom, N. J. Smith and E. M. Heimlich. A. M. A. J. Dis. Child. 92:219-253 (Sept.) 1956 [Chicago].

Four infants under 8 months of age with an unusual syndrome of edema, irritability, and pallor were studied during an 18-month period. All four were born at term, had had an optimal diet, and had no laboratory evidence of renal or hepatic disease. Marked hypoproteinemia was present in each patient at some time during the illness. The age of onset of symptoms ranged from less than 1 month to 7 months. The disease was apparently self-limited, with spontaneous recovery occurring in each infant between the 7th and 9th months of life. The striking similarity of the clinical findings in these patients suggests a single disease process. The extensive studies reported here seem to indicate that an abnormality in protein metabolism at the cellular level is responsible. The normal dietary intakes during the development of anemia and hypoproteinemia and the spontaneous return to normal without recognizable changes in the diet, as well as the many studies presented here, indicate that this disturbance was not primarily of dietary origin. The evidence at hand does not permit assignment of a definite etiological factor, although the mechanism for the development of signs and symptoms seems clear.

DERMATOLOGY

Malignant Blue Nevus. E. R. Fisher. A.M.A. Arch. Dermat. 74:227-231 (Sept.) 1956 [Chicago].

A 27-year-old white man first noticed a pinhead-sized blue nodule in the right occipital region of the scalp at the age of 17. Four years later he noted a progressive enlargement of the lesion and a mass in the right cervical region. Biopsy of the latter revealed a secondary malignant melanoma within a lymph node. The pigmented lesion of the scalp was excised, and a radical dissection of the right cervical lymph nodes was performed. The patient remained in good health during the next six years, but three months before hospitalization he noted a 20-lb. weight loss and numerous pigmented and nonpigmented nodules on the skin of the neck, back, and abdomen. There was weakness, anorexia, and moderately severe pain in the right upper abdominal quadrant. Examination revealed the liver to be enlarged and nodular. In addition to the cutaneous nodules, which varied in size from several millimeters to 1 cm. in cross diameter, several lymph nodes in the posterior cervical chain on the right were also palpably enlarged.

A needle biopsy of the liver was performed, and one of the subcutaneous nodules was excised. The clinical and morphological features of the malignant melanoma removed from this patient's scalp indicate its origin from a blue nevus. The vacuolation of the tumor cells, carcinomatous configuration, and nuclear pleomorphism and occasional mitotic figures are considered diagnostic of malignancy in lesions presenting other features of the blue nevus. It is interesting to note that the morphological appearance of the metastatic lesions in the subcutaneous tissue and liver did not possess features that would enable one to establish their derivation from the blue nevus. The tumor cells were spindle-shaped, without vacuolation, and resembled other malignant melanomas not arising in blue nevus. The vacuolation of the tumor cells observed is not unlike the change noted in the tumor cells of some melanomas during pregnancy. Such cytological alteration suggests a hormonal influence upon the tumor cells of this lesion, although this patient did not reveal any overt clinical manifestations of endocrine imbalance. The significance and nature of the asteroid bodies observed within the cytoplasm of some of the tumor cells of the present malignant blue nevus are not apparent. As far as the author was able to ascertain, such structures have not previously been recorded in pigmented tumors of the nevus-melanoma type.

Necrobiosis Lipoidica: A Disease of Changing Concepts. J. Graham Smith Jr. A.M.A. Arch. Dermat. 74:280-285 (Sept.) 1956 [Chicago].

The author analyzed the records of 19 patients with necrobiosis lipoidica seen at Duke Hospital. Data obtained on these 19 patients were compared with tabulated data from 34 of a total of 52 cases of necrobiosis lipoidica reported in the A.M.A. *Archives of Dermatology and Syphilology* during the past 10 years. Regarding the 19 cases, he says that in only one-fourth of these was necrobiosis lipoidica associated with diabetes mellitus even when patients with equivocal but not definitely diabetic glucose-tolerance curves were included in the diabetic group. When diabetes mellitus is associated with necrobiosis lipoidica, the diabetes mellitus usually develops first; however, the association of diabetes mellitus apparently does not alter significantly the age of onset for necrobiosis lipoidica. In reviewing the slides from 13 of the 19 patients, it was found that in only 4 of the 13 did there seem to be a resemblance to granuloma annulare, and so the author concludes that necrobiosis is probably not a variant of granuloma annulare.

Approximately 90% of cases of necrobiosis lipoidica occur in women; the Negro and Oriental races are rarely affected if at all, and the disease, while more commonly having its onset in young adults, occurs in all age groups except in infancy and early childhood. Lesions are not frequently seen in locations other than the lower extremities. Ulceration probably occurs more frequently in diabetics, but it may occur in nondiabetics. Mucous membrane lesions do not occur. The etiology of necrobiosis lipoidica is obscure, but the pathological changes are probably secondary to vascular abnormalities. Surgical excision with grafting if necessary to close large defects is the most effective therapy available at present. Intralesional injection of hydrocortisone deserves further trial.

Nickel Dermatitis. H. T. H. Wilson. Practitioner 177:303-308 (Sept.) 1956 [London, England].

This report is concerned with dermatitis resulting from contact with nickel or nickel-plated articles. Nickel-plated articles, such as the metallic parts of garters, are nearly always barrel plated: that is to say, they are nickel plated in an acid nickel solution in a rotating barrel. The thickness of nickel deposited is usually of the order of 0.0002 in. (0.05 mm.). When the plating process is complete, the articles are washed in hot water. Unless the washing is adequate, the plated articles are likely to become coated with a thin film of nickel salts. This may account for the fact that dermatitis often seems to develop for the first time soon after the wearing of a comparatively new nickel-plated buckle or clasp. In the present series of 85 women, 12 out of 22 stated that their dermatitis arose beneath a nickel-plated article purchased a month or less previously. The rash began as a localized dermatitis, usually at the back of the thighs, at the point of contact with the garter buckles. Less frequently it began under a wrist watch, necklace clasp, or earring. Swelling and redness of the eyelids sometimes preceded all other symptoms, and occasionally a chronic papular eruption developed on the elbow flexures or axillary folds before the onset of lesions elsewhere. In only two patients did the rash remain localized to a single area. In the remainder, after a few weeks or months, eczematous patches developed on other parts of the body. Nickel dermatitis appears to consist of two separate components: a simple dermatitis localized to the area of nickel contact, and a chronic eczema or neurodermatitis having no obvious connection with such contact. These two components are so intimately associated that the diagnosis of suspender dermatitis can often be made on seeing the characteristic papular rash on the patient's elbow flexures.

All patients were patch-tested against metallic nickel and solutions of nickel sulfate. In every case strongly positive reactions were observed to nickel sulfate (2.5%), and severe reactions followed the few tests made with higher concentrations. It would appear from serial tests that a 1% solution is a suitable strength for patch testing and solutions stronger than 2.5% should not be used. Metallic nickel gave a reaction equal to 0.5 or 1% of the solution. Complete removal of all metal clasps and buckles did not suffice to prevent relapses in every case. Nickel sensitivity, once acquired, is likely to persist.

INDUSTRIAL MEDICINE

Silage Gas Poisoning: Nitrogen Dioxide Pneumonia, a New Disease in Agricultural Workers. R. R. Grayson. Ann. Int. Med. 45:393-408 (Sept.) 1956 [Lancaster, Pa.].

Two patients with acute respiratory disease due to inhalation of silage gas were observed by the author in August, 1954. One died. A thorough investigation of these two cases and of the silage gas that caused the illness indicates that the disease was caused by the oxides of nitrogen and is essentially a diffuse chemical bronchopneumonia caused by the irritating action of nitrous and nitric acids on the respiratory tree. The disease may be mild or severe, depending upon the degree of exposure. Nitrogen dioxide pneumonia has been described many times in industrial toxicology but has apparently not been previously described in the medical literature as due to inhalation of gases from ensilage. Special studies carried out on the corn ensilage and on the actual gas from the silo in which the two patients were poisoned proved that there was a poisonous concentration of the oxides of nitrogen. This condition was due to a combination of drought, high-nitrate soils, and an unventilated silo. Other studies demonstrated the toxicity of the actual gas and of experimentally produced gas from the same ensilage. Silage gas poisoning due to the oxides of nitrogen with the production of chemical pneumonia is a disease that probably occurs more commonly than is recognized. Physicians in rural areas should be aware of the possibility of this disease during summer periods when corn is being placed in silos, particularly during times of drought. No specific treatment is known for the resulting bronchopneumonia. Research should be directed toward the discovery of a specific therapy.

PATHOLOGY

Cushing's Syndrome in Children Associated with Adrenal Cortical Carcinoma: A Case Report with Review of the Literature. G. H. Guin and E. F. Gilbert. A. M. A. J. Dis. Child. 92:297-307 (Sept.) 1956 [Chicago].

A 3-month-old girl was admitted to the Children's Hospital of the District of Columbia because of obesity beginning 6 weeks before admission. For three weeks before admission the patient was noted to have an eczematoid and acne-form rash on the cheeks. The infant was obese, showing a buffalo hump and moon face. There was no axillary or pubic hair and no abnormality of the external genitalia other than slight clitoral hypertrophy. There was hirsutism of the upper lip and an erythematous papular rash over the face and neck. The abdomen was distended, and the liver was palpable. A firm mass unattached to the liver was palpated to the right of the umbilicus. X-ray examination revealed marked osteoporosis of the entire skeletal system. Exploratory laparotomy revealed a tumor replacing the right adrenal, which was removed. The infant died on the fourth postoperative day after several episodes of apnea. Examination of the surgical specimen established the diagnosis of cortical carcinoma of the right adrenal.

Twenty-eight cases of adrenal cortical carcinoma associated with Cushing's syndrome in children under 14 years of age were collected from the literature. The reported case is believed to concern the youngest patient with adrenal cortical carcinoma on record. The fact that the mother of this infant had diabetes is considered to be of special interest. Of the 29 tabulated cases, 20 occurred in females and 9 in males. Eighteen patients died, and all but one of these came to autopsy. Histological confirmation of adrenal cortical carcinoma in this patient had been obtained surgically. Nine patients underwent surgical treatment. Persistent elevations of plasma and urinary 17-hydroxycorticosteroids and urinary 17-ketosteroids after ACTH stimulation provide an additional aid for the diagnosis of adrenocortical carcinoma.

THERAPEUTICS

Hydergine (a Vasodilator): Clinical Report on Hydergine in Peripheral Vascular Disease. W. deHaven Stick. Pennsylvania M. J. 59:1072-1074 (Sept.) 1956 [Harrisburg, Pa.].

Having found that vasodilating agents such as tetraethylammonium chloride, Priscoline, and Ilidar phosphate were inadequate in the treatment of functional or organic occlusive vascular disease of the lower extremities, the author tried hydergine, an equiproportional mixture of the three hydrogenated alkaloids of the "ergotoxine group," namely, ergocristine, ergocornine, and ergokryptine. Nearly 2000 oral and 200 parenteral doses of hydergine have been given in the course of the last six months to about 20 patients at the New York Hospital. The majority of these patients with arteriosclerotic obstructive vascular disease were in the 55 to 75 year age group. Pallor, atrophy, reduced temperature, cyanosis, intermittent claudication, early digital necrosis, nocturnal ischemia, and frank gangrene of one or more digits were the characteristic symptoms. The drug was also given to a few patients with functional obstruction as seen in association with thrombophlebitis, phlebothrombosis, hyperhidrosis, and, in one patient, frostbite residuum. All routes of drug administration were utilized in nearly every patient, including the oral, sublingual, parenteral, and direct intra-arterial routes. The drug was given to each patient for at least six days.

Only five patients obtained palliative benefit from treatment with hydergine, and only one patient showed actual progress in healing. Hydergine with Ilidar may be indicated in acutely painful ischemia of the lower limbs as a preliminary or adjunct to surgical treatment. Hydergine, given intravenously, appears to be a drug of choice in coping with acute hypertensive phenomena precipitated by the injection of radiographic substances for diagnostic procedures. Medical sympathectomy by the use of vasodilating agents, including hydergine, is of slight value in the management of peripheral vascular disease. Surgical sympathectomy remains the method of choice when warranted.

The Combination of Reserpine with Methyl-Phenyl-Piperidine Acetate in the Treatment of Hypertension. G. Visco. Clin. terap. 11:11-32 (July) 1956 (In Italian) [Rome, Italy].

Reserpine has several side-effects and is ineffective in many types of hypertension. Methyl-phenyl-piperidine acetate (A. M. F. P.) has a central sympathomimetic stimulant effect and a mild sympathicoperipheral effect. A combination of the two drugs was used in the treatment of 23 patients with hypertension who were followed for from 1 to 14 months after the treatment. They were between 18 and 73 years of age (average age, 49.8 years). Eighteen patients had essential hypertension, 3 had malignant hypertension, and 2 had chronic nephritis in a preuremic state. Ten patients (43.4%) showed a great reduction in the pressure values. The decrease in the systolic pressure was marked; the decrease in the diastolic pressure was less marked but more constant. A. M. F. P. did not interfere with the hypotensive effect of reserpine, but did prevent its side-effects: drowsiness, asthenia, psychic torpor, and vertigo. Bradycardia, nasal congestion, and hypothermia were also somewhat checked with the use of A. M. F. P. The collateral effects, such as the increase in the appetite and body weight, were less marked but still very significant. The two drugs had a synergistic effect on the patients' euphoria and the incidence of tremor, diarrhea, and night dreams.

In another experiment the authors gave a dose of 15 mg. per day of A. M. F. P. to 13 patients who were being treated with high doses of reserpine. The effects of A. M. F. P. on side-effects were less evident: 10 of the 13 patients had bradycardia, 9 had asthenia and mental torpor, and 7 had nasal stuffiness. Treatment had to be discontinued in 4 patients who were receiving the drug by intramuscular injection.

Severe Hypoglycemic Reactions in the Course of Treatment of Diabetes Mellitus with Carbutamide (BZ-55). E. Bendfeldt and H. Otto. München. med. Wchnschr. 98:1136-1137 (Aug. 31) 1956 (In German) [Munich, Germany].

Severe hypoglycemic reactions to carbutamide (BZ-55) occurred in 2 of 740 patients with diabetes mellitus who were treated with this drug. The patients were adipose women aged 59 and 70 years who were given 5 tablets of the drug on the first day of the treatment, 4 tablets on the second day, 3 tablets on the third day, and 2 tablets on successive days. In the younger patient, who had hypertension, cardiac decompensation, and diabetic nephropathy and who had been treated with insulin for many years, the fasting blood sugar level varied between 230 and 310 mg. per 100 cc. before the institution of carbutamide therapy; it dropped to 105 mg. per 100 cc. on the 10th day of treatment, when drowsiness and a mild right facial paresis occurred. In the evening of the same day the patient became unconscious and the blood sugar level dropped to 35 mg. per 100 cc. The patient became conscious within a few minutes after the intravenous administration of 40 gm. of dextrose, (in 50% solution), and the neurological symptoms disappeared completely. Despite the administration of carbohydrates, the blood sugar level still bordered on hypoglycemia 27 hours after the last carbutamide tablet had been given. In the older patient, who had severe general atherosclerosis and who had been admitted to hospital for sclerotic gangrene in the right foot, the presence of diabetes mellitus had not previously been recognized, but the blood sugar level on admission was found to vary between 177 and 242 mg. per 100 cc. On the third day of carbutamide therapy the fasting blood sugar level had dropped to 90 mg. per 100 cc., when the patient became drowsy, confused, and finally unconscious with rattling breathing. An apoplectic attack was considered and the patient was given aminophylline and 10 gm. of dextrose, and after that her responsiveness was somewhat improved. The diagnosis of a hypoglycemic reaction was established by the determination of a blood sugar level of 70 mg. per 100 cc. Consciousness was restored completely after the intravenous administration of an additional 25 gm. of dextrose, but five hours later she again became unconscious. Consciousness was restored once more by the intravenous administration of 25 gm. of dextrose, and after that she was given 15 gm. dextrose orally every hour.

In these two patients, the insidious and protracted course of the condition and the central nervous manifestations, which dominated the clinical picture and which subsided within a short time after the intravenous administration of dextrose, reminded one of hypoglycemic shock after the administration of long-acting insulin. Both patients had other diseases in addition to diabetes. Preuremia with residual nitrogen values of 60 mg. per 100 cc. was present at the onset of hypoglycemia in both patients. Determinations of carbutamide in the blood and urine of the older of the two patients showed that the carbutamide blood concentration was within the usual limits 24 hours after the onset of hypoglycemia and that the carbutamide excretion in the urine was not reduced as compared with that in patients without renal impairment who had received the same dose of the drug. These findings suggest that at least in this patient renal impairment did not inhibit the excretion of carbutamide in the urine and, therefore, did not cause an accumulation of the drug in the blood that could have been responsible for the hypoglycemia. Patients with diabetes of long duration associated with severe late complications, as in the younger woman, may have a tendency to pronounced variations in their blood sugar level, and hypoglycemia may result from insignificant causes.

RADIOLOGY

Carcinoma of the Lip. P. M. Burke and F. S. Hopkins. New England J. Med. 255:552-555 (Sept. 20) 1956 [Boston].

During the 12-year period from 1938 through 1950, 225 patients with cancer of the lip were seen in the cancer section of the Westfield State Sanatorium. This report is based on an analysis of the 182 patients who received their primary treatment at this institution. All lesions were histologically proved squamous-cell carcinoma, and all patients have been followed for over five years. All except 6 of the 182 patients were men. Treatment consisted of surgical removal of the tumor in 69 patients, while 97 patients received only irradiation treatment and 16 received a combination of surgical and x-ray therapy. One hundred eighteen (65%) of the 182 patients survived for five years without recurrence. The five-year survival rate is 80% when it is adjusted for the 35 patients who died within five years of other causes without recurrence of cancer. This compares well with the five-year cure rate reported by others. There is considerable difference of opinion in the literature about the best method of treating the primary lesion. Surgical therapy is favored by some and irradiation by others. The authors found that primary lip cancers comparable in size and histological grade respond about as well to x-ray as to surgical therapy. When an enlarged lymph node is present, the extent of the neck dissection should be decided on an individual basis. Routine neck dissection for cancer of the lip without enlarged lymph nodes is not recommended.

Primary Chickenpox Pneumonia. D. Y. M. Tan, S. A. Kaufman and G. Levene. Am. J. Roentgenol. 76:527-532 (Sept.) 1956 [Springfield, Ill.].

It is not generally realized that the varicella virus is capable of producing such complications as pneumonia, encephalitis, and nephritis. Only 15 well-documented cases (including four fatal ones) of chickenpox pneumonia have appeared in the literature up to 1955. The authors present observations on 16 patients seen at the John Haynes Memorial of the Massachusetts Memorial Hospitals. Pneumonia as a complication of chickenpox occurred in adults over the age of 19 with one exception, a 5-year-old girl. The onset of the respiratory symptoms occurred within five days of the appearance of the rash. The rash was severe, and in most patients confluent over the whole body. Vesicles were also found in the mouth and pharynx. The patients were acutely ill, with temperatures of from 101 to 105 F (38 to 41 C). They had severe cough and several had hemoptysis. Half of them had chest pain and dyspnea. Physical examination of the chest was generally not remarkable despite the extensive roentgen changes. Three patients had generalized lymph-node enlargement. The white blood cell count was elevated in slightly less than half of the cases, but the differential count remained normal in all.

The roentgenologic changes showed a characteristic pattern. There were widespread nodular densities superimposed on increased bronchovascular markings. These infiltrates varied in size, and though some were sharply defined from the surrounding lung others seemed to merge with the adjacent tissue. Transitory changes were common, and the disease, in some cases, changed rapidly, some areas of infiltration resolving while others appeared. In a few instances there was a tendency for the nodules to coalesce so that there appeared to be patchy areas of consolidation. This was most noticeable ot the lung bases. No portion of the lung was spared, although the densities seemed heaviest about the hilum and gradually diminished toward the periphery. While an etiological diagnosis of pneumonia is not possible from the roentgenologic examination alone, it has been the experience of these authors that these striking findings in a patient with chickenpox can be taken as presumptive evidence of primary varicella pneumonia. This can usually be confirmed by clinical and laboratory findings. Various chemotherapeutic agents were tried without success, the disease varying in duration from a few days to two weeks. There were no fatalities.

Therapy of Dupuytren's Contracture. K. Wasserburger. Strahlentherapie 100:546-560 (No. 4) 1956 (In German) [Munich, Germany].

At the department for irradiation therapy of a Vienna Hospital efforts have been made to develop an effective radium therapy for Dupuytren's contracture. Radium therapy is carried out with an apparatus for distant therapy, which is a circular arrangement of eight barrel-shaped holders, each of which contains 50 mg. radium element. The 400 mg. of radium element are filtered through 1 mm. of platinum. Lateral shielding is provided by 4 cm. of lead. The instrument is mounted in such a way that the effective cone of rays can be directed and fixed in any desired position. The radium-skin distance in the treatment of Dupuytren's contracture was 2 cm. The size of the field of treatment was 5 sq. cm. Depending on the extent of the lesion and on whether one or several fingers was involved from three to five fields were irradiated on each hand. If necessary the series of treatments was repeated after from three to six months.

Irradiation treatment was applied to 213 patients with Dupuytren's contracture during the years from 1937 to 195 The irradiation was the primary treatment in 185 of thes patients, the remaining 28 having first received surgical treatment. Follow-up studies on 146 of the 185 patients revealed that in 102 the results were very good, 24 others obtained improvement, and the remaining 20 experienced no improvement.

In classifying the lesions according to the degree of severity and advancement, it was found that of the patients with stage 1 lesions, 89.8% were cured; of those with stage 2 lesions, 56.5%; and of those with stage 3 lesions, 32.2%. This indicates the importance of early treatment.

Angiocardiography in the Preoperative Diagnosis of Mitral Stenosis and Insufficiency. J. G. McAfee, T. F. Hilbish and K. R. Stewart. Radiology 67:321-331 (Sept.) 1956 [Syracuse, N. Y.].

The authors performed angiocardiography in 50 patients with mitral rheumatic heart disease, but this report is concerned only with the 32 surgically proved cases. Although the surgical correction of mitral stenosis has become firmly established, that of mitral regurgitation has remained largely experimental. In the preoperative evaluation of patients, therefore, the accurate differentiation of stenosis from insufficiency is of the utmost importance. Angiocardiography is not a reliable procedure for distinguishing between mitral stenosis and insufficiency. The diagnostic accuracy was poorer than that of conventional clinical methods. Both false-positive and false-negative diagnoses of mitral stenosis were made. In this, as in other unselected series, patients with stenosis predominated. The problem of selecting the small minority with predominant insufficiency has not been solved by angiocardiography. No difference in the "opacification pattern" of the left atrium and ventricle was observed in stenosis and insufficiency that could not be explained on the basis of chamber size and cardiac phase. The prolonged opacification of the left atrium seen in mitral disease is due to its large size and generalized slowing of the circulation. In the absence of shunts, the output (volume per unit time) in all chambers of the heart remains equal; there is no specific "hold-up" of the contrast medium in the left atrium by a stenotic mitral valve. Angiocardiography is of value in demonstrating the size and position of the cardiac chambers, but this can usually be assessed by ordinary roentgenographic means. Left ventricular enlargement was demonstrated in only two of five patients with proved "pure" mitral insufficiency. It may be possible in the future to visualize the mitral valve orifice by selective angiocardiography performed through a direct left atrial puncture.

Congenital Cystic Adenomatoid Malformation of the Lung in Infants. J. M. Craig, J. Kirkpatrick and E. B. D. Neuhauser. Am. J. Roentgenol. 76:516-526 (Sept.) 1956 [Springfield, Ill.].

Formation of cysts related to alveolar and interstitial emphysema is frequent in early life in infants suffering from neonatal asphyxia associated with the formation of hyaline membranes and in those with pneumonia, due to Streptococcus pyogenes. Cysts of this origin usually resorb quickly and without sequelae. Infants with indisputably congenital cystic malformations have been observed at the Children's Medical Center of Harvard University over the past 25 years, in whom the structure of the cystic lungs was such that it was inconceivable that they would ever function normally or that the cysts would disappear spontaneously. In the four cases reported, surgical extirpation was carried out in the first two weeks of life. They presented the identical features described by Ch'in and Tang as "congenital adenomatoid malformation." All four infants had similar signs and symptoms, consisting of cyanosis, rapid respirations, and an absence of respiratory distress or fever. The physical signs were those of displacement of the mediastinum to the side opposite that of the affected lung, dulness to percussion over the affected lung, and diminished breath sounds over this area. The roentgen signs in all four infants were those of an intrapulmonary mass of soft-tissue density, containing scattered radiolucent areas. The outlines of the mass were usually quite sharp and the malformation was limited to one lobe. A roentgenogram taken very early in life may show only the presence of a soft-tissue density without any radiolucent air-containing areas, at a time before any air has penetrated the honeycombed mass. At operation, the mass was usually well defined. The anatomy of the lesion is striking because of the great increase in size and weight of the affected portion, many of the affected lungs being twice the usual dimensions and weight.

Since in two of the infants the involved lungs increased rapidly in size with a concomitant increase in the air-containing cystic structures with further displacement of the mediastinum and compromise of respiratory function, it appears that once a definite diagnosis of such adenomatoid cystic malformations is made, surgical treatment is mandatory. It proved effective in three of the four infants, but the fourth infant died two days after the operation. Congenital cystic adenomatoid malformation should not be confused with either the accessory lung, which has no connection with the bronchial system or pulmonary blood supply, or with the sequestrated lobe, which is usually connected with the bronchial system but derives its blood supply from a branch of the aorta.

PHYSIOLOGY

A Comparison of the Biological Values of Dietary Protein Incorporated in High- and Low-Fat Diets. V. C. Metta and H. H. Mitchell. J. Nutrition 59:501-513 (Aug.) 1956 [Philadelphia].

The effect of fat as compared with that of isocaloric amounts of carbohydrate on nitrogen utilization in the severely protein-depleated and the growing rat was investigated. The low-fat and the high-fat diets contained, respectively, 5 and 33% fat, mainly lard. Casein was the dietary protein tested. The rats were fed the test diets so that they received equal amounts of protein, crude fiber, vitamins, minerals, and gross energy, the main difference between the two groups being in the fat intake. When fed in isocaloric amounts, dietary fat and carbohydrate had essentially the same effect on protein utilization in both the protein-depleted rat and the growing rat. Neither the apparent digestibility nor the true digestibility of casein was improved by the higher dietary fat level. Fat did not seem to spare endogenous nitrogen under conditions of satisfactory and equal caloric intake. Higher dietary fat levels did not improve the biological value of casein. In fact, the indications in one experiment were that a high-carbohydrate diet tends to improve the biological value of casein in the protein-depleted rat. The metabolic fecal nitrogen per gram of food intake increased significantly when the dietary fat was increased because of a concomitant reduction in the food intake due to isocaloric feeding. This value, however, remained constant irrespective of the fat content of the diet when the rats were fed equal amounts of the low-fat and the high-fat diets.

The Determination of Chromosomal Sex by Oral Smears. W. Herrmann and A. M. Davis. Yale J. Biol. & Med. 29:69-74 (Sept.) 1956 [New Haven, Conn.].

Oral smears were obtained from 100 persons of varying ages for a control series. Fifty men and 50 women each had the buccal mucosa scraped with a wooden spatula. The material obtained was smeared on a glass slide and immediately dropped into a solution containing equal parts of ether and 95% ethyl alcohol. The slides were then stained with the Papanicolaou stain. Each slide was studied under an oil immersion lens, and the sex chromatin was easily identified. The sex of the person from whom the specimen was obtained was not known until after the counts had been made.

The authors then applied the test to 15 patients whose true sex was questionable. Four of these patients had been given a clinical diagnosis of pseudohermaphroditism, three being considered anatomically female and one anatomically male. One of the three females had proved congenital adrenal hyperplasia, with a diagnosis confirmed by the elevated beta fraction of the 17-ketosteroids. The other two were newborn twins on whom no endocrine essays had as yet been performed. These twins showed a phallus-like development of the clitoris. All three patients had a female chromosomal pattern. The anatomically male pseudohermaphrodite was 44 years old and had previously been given a diagnosis of a male achondroplastic dwarf. A chromatin count indicated that this patient was genetically female. Two of the patients with gonadal dysgenesis proved to be chromosomally male, even though they had female genitalia and were living satisfactory lives emotionally, physically, and mentally as females. The true hermaphrodite had female external genitalia, a testis on one side and an ovary on the other, and a chromatin count following a female pattern. In the remaining cases the chromosomal sex corresponded with the anatomic sex.

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At the department for irradiation therapy of a Vienna Hospital efforts have been made to develop an effective radium therapy for Dupuytren's contracture. Radium therapy is carried out with an apparatus for distant therapy, which is a circular arrangement of eight barrel-shaped holders, each of which contains 50 mg. radium element. The 400 mg. of radium element are filtered through 1 mm. of platinum. Lateral shielding is provided by 4 cm. of lead. The instrument is mounted in such a way that the effective cone of rays can be directed and fixed in any desired position. The radium-skin distance in the treatment of Dupuytren's contracture was 2 cm. The size of the field of treatment was 5 sq. cm. Depending on the extent of the lesion and on whether one or several fingers was involved from three to five fields were irradiated on each hand. If necessary the series of treatments was repeated after from three to six months.

Irradiation treatment was applied to 213 patients with Dupuytren's contracture during the years from 1937 to 1953 The irradiation was the primary treatment in 185 of these patients, the remaining 28 having first received surgical treatment. Follow-up studies on 146 of the 185 patients revealed that in 102 the results were very good, 24 others obtained improvement, and the remaining 20 experienced no improvement.

Handbook of Legal Medicine. By Louis J. Regan, M.D., LL.B., Professor of Legal Medicine, University of Southern California, Los Angeles, and Alan R. Moritz, M.D., Professor of Pathology, Western Reserve University, Cleveland. Cloth. $3.90. Pp. 201, with 11 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1956.

For many years the need in our medicolegal library for a short, simple, concise review of the many subjects referred to under the heading of medical jurisprudence and the various aspects of scientific medicolegal investigations has been recognized. In this book two of the outstanding experts in the United States have discussed these subjects in an understandable and acceptable form to medical and legal students. Unfortunately the average student of law or of medicine has had little or no opportunity to study these subjects during his regular academic schedule. When in the past the need arose or the desire existed to study in this field, the student has been discouraged by the voluminous and technical nature of published material. This obstacle has now been removed. The book will also provide a useful working manual for practicing lawyers and physicians. While it is true that for the few who are expert in these two fields the material presented will be elementary, for most lawyers and physicians, it will be a valuable and useful guide.

Dr. Regan tends to dicuss many subjects in terms of medical professional liability rather than in relation to the broader field of personal injury litigation. Although this approach may mislead some readers as to the importance or significance of some of the subject matter, it has not apparently resulted in any inaccuracies or misstatements. The second portion of the book should be of great value to students and physicians, but it should be particularly helpful to attorneys who are confronted with the investigation, prosecution, or defense of cases involving violent crimes or disputed paternity. This section of the book should provide them with a clear and authoritative commentary on the major aspects of these subjects. The book includes an extensive glossary of medical and legal terms, a detailed table of contents, and a bibliography of selected references in the medicolegal field. This book should be widely circulated not only for the education and edification of students, lawyers, and physicians but also as an important aid in the better administration of justice in civil and criminal cases.

Head Injuries and Their Management. By Francis Asbury Echlin, M.D., C.M., M.Sc., Professor Clinical Neurosurgery, New York University, Postgraduate Medical School, New York. This material was published in American Practitioner and Digest of Treatment for May, 1956. Cloth. $3. Pp. 127, with 10 illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; 2083 Guy St., Montreal, Canada; Pitman Medical Publishing Company, Ltd., Pitman House, 39-41 Parker St., Kingsway, London, W.C.2, England, 1956.

The book, which is small enough to slip into a coat pocket, is a brief description of the essentials in diagnosis and treatment of head injuries for residents and the practicing surgeon and physician. There are succinct chapters on the mechanisms of head injury, nonsurgical lesions of the brain, surgical conditions such as hematomas, scalp wounds, skull fractures, penetrating wounds of the brain, and a few paragraphs on infections and other complications, including post-traumatic epilepsy, cerebral palsy, the post-traumatic syndrome of headache, "dizziness" and nervousness, and neuroses, psychoses, and rehabilitation. Discussions of pneumography, angiography, and electroencephalography are so brief as to be of no particular value. A good selective bibliography and an adequate index conclude the volume. Within its limited aims, the volume contains no serious errors except those of omission. Precisely, it is a primer, of limited value for students, interns, and residents. There is nothing here for neurologists or neurosurgeons and nothing to equip a general surgeon for the surgical management of head injuries. It rightly points out that over 97% of closed head injuries require no operation and presents admirably the generally accepted criteria for diagnostic appraisal, observation, and management. As any primer must, it lacks important surgical details, and, even for so brief a manual, it is inadequate in its discussion of all the nonsurgical aspects of head injuries such as the post-traumatic syndrome, pneumography, angiography, and the electroencephalogram. No account is given of the medical treatment of post-traumatic convulsive states. Discussion of the post-traumatic neuroses and psychoses is passed over entirely. The book is thus grossly inadequate; perhaps any brief presentation of the problems of head injuries must be inadequate. To make the complex simple is a most dubious enterprise, as this book amply demonstrates.

Industrial Medicine and Hygiene. Volumes I-III. Edited by E. R. A. Merewether, C.B.E., O.St.J., M.D., H.M. Senior Medical Inspector of Factories, Ministry of Labour and National Service, [London, England.] With foreword by The Lord Horder, G.C.V.O., M.D., F.R.C.P. Cloth. Pp. 426, with 33 illustrations; 451, with 81 illustrations; 617, with 57 illustrations. F. A. Davis Company, 1914-1916 Cherry St., Philadelphia 3; Butterworth & Co., Ltd., 88 Kingsway, London, W.C.2, England; 1367 Danforth Ave., Toronto 6, Canada, 1954; 1956.

This is an ambitious work, as indicated by its title. It comprises three volumes, lists about 1,500 references to the pertinent European and American literature, and contains sections from over 30 contributors representing medicine, pharmacology, toxicology, chemistry, psychology, nursing, industrial hygiene, civil and electrical engineering, law, and management. Besides industrial medical directors and governmental plant inspectors, the physicians contributing include public health specialists, internists, ophthalmologists, otolaryngologists, dermatologists, and some who are lawyers as well. The first volume should be of particular value to the British reader, inasmuch as it presents the background and basis, in British history and law, of workmen's compensation and of programs of industrial health and rehabilitation and the organization and statistics of health services of various British industries. The American reader will derive greater profit from a study of the other two volumes. Volume II deals with occupational skin diseases, ophthalmology, psychology, compressed air, heating, ventilation, lighting, noise, ionizing radiation, and industrial accidents. It discusses the causes, prevention, and in some instances the treatment of harmful effects from these agents and influences. Volume III, far thicker than either of the other volumes, deals with silicosis and other pneumonoconioses, industrial carcinogenesis, and toxicology. It offers an exhaustive but, for the average physician, somewhat hard-to-understand account of the chemistry, enzyme reactions, and derangements involved in the various industrial intoxications. This work is well written. It is an authentic source of valuable information; guidance, especially for the British; and references, particularly on industrial and compensation medicine, rehabilitation, toxicology, and, to a lesser extent, industrial hygiene.

British Postgraduate Medical Federation, University of London, Lectures on the Scientific Basis of Medicine. Volume IV: 1954-55. Cloth. $6.50. Pp. 397, with 34 plates. Athlone Press, University of London, 2 Gower St., London, W.C.1, England, John de Graff, Inc., 31 E. 10th St., New York 3, 1956.

This volume contains 21 lectures, most of them very interesting, on a variety of medical subjects; each is by a different speaker. It will probably be most appreciated by medical students as a book to be picked up from time to time to furnish inspiring sidelights on anatomy, biochemistry, and physiology. A chapter on the chemistry of the porphyrias, for instance, includes photographs showing the devastating physical effects of this metabolic disease. A chapter on nucleoproteins in cell structure shows how the ability of these complicated, three-dimensional molecules to duplicate themselves is involved in most processes of growth and reproduction. A chapter on the cooling of the whole organism gives recent results on artificial hibernation, considers the danger and prevention of cardiac fibrillation in hypothermia, and sketches possible applications in surgery. The chapter on alcohol contains much scientific information enlivened by a discreet touch of humor. Other topics that will appeal to the medical student include the chemical aspects of abnormal growth, shock from burns, radiation injury to bones, and the effects of distention of viscera. The book also offers chapters that will be especially appreciated by physicians seeking coherent summaries of recent developments in the basic sciences; some of these chapters are entitled The Plasma Proteins, Laboratory and Clinical Findings in Hypersensitivity, Reaction of Enzymes to Injury, and Fat Metabolism. The book lacks an index, but each chapter includes a bibliography. The illustrations are excellent.

The Practice of Psychosomatic Medicine as Illustrated in Allergy. By Hyman Miller, M.D., *Associate Clinical Professor of Medicine, University of California at Los Angeles, Los Angeles, and Dorothy W. Baruch, Ph.D.* Cloth. $5. Pp. 196. *Blakiston Division,* McGraw-Hill Book Company, Inc., 330 W. 42nd St., *New York 36; 95 Farringdon St., London, E.C. 4, England, 1956.*

This book, *written by an allergist and* psychologist, is mistitled, for it is not a treatise on the practice of psychosomatic medicine but rather a monograph on the psychosomatic approach to allergy. Its focus is on allergic patients, and, although much significant information is contained about the role of the psyche in the sufferings of such patients, general applications for the whole field are not discussed. The authors contend that the allergic patient, like any sick person, can only be understood in the context of his total family situation. Both the allergic constitution and the emotional climate of the family are significant in the production of the disease. Emotional factors act as trigger mechanisms for the production of the symptoms. The task of diagnosing these factors in adults and children requires special technical procedure, and their treatment is effected by means of special skills not transmitted through reading. The book is simply written and easily understandable. The authors recognize that emotional factors are but a part of the total allergic syndrome, and this part they present well. Reading the book may stimulate allergists to obtain more *training in psychodynamics or to greater* willingness for cooperation with psychiatrists. The bibliography and index are barely adequate.

Surgical Forum. Volume VI. Proceedings of Forum Sessions, Forty-First Clinical Congress of the American College of Surgeons, Chicago, Illinois, November, 1955. *Surgical Forum Committee:* Harris B. Shumacker, Jr., *chairman,* and others. Cloth. $5. Pp. 654, with illustrations. American College of Surgeons, *40 E. Erie St., Chicago 11, 1956.*

Beginning with this volume, the American College of Surgeons has itself assumed responsibility for publication of the annual "Surgical Forum." The contributions cover the fields of general surgery, neurosurgery, gynecology and obstetrics, orthopedics, plastic surgery, and urology. The contents of the volume reflect most of the advances in these fields and point toward further studies in clinical surgery. The printing, binding, and illustrations are of the same excellence that characterized the previous volumes.

Joint Ligament Relaxation Treated by Fibro-Osseous *Proliferation.* By George Stuart Hackett, M.D., F.A.C.S., Consulting Surgeon, Mercy Hospital, *Canton, Ohio. With special reference to low back disability—trigger point pain and referred pain.* Cloth. $4.75. Pp. 97, with 17 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell *Scientific* Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson *Press,* 299 Queen St., W., Toronto 2B, Canada, 1956.

This monograph propounds the theory that most backache and pain in or about other joints is due to chronic relaxation of ligaments. While it is true that chronic relaxation of ligaments may and does at times produce localized and referred pain, such as the author has described and treated by his method of injection, there are many other conditions, such as fibrositis, bursitis, or chronic edema at the insertion of ligaments or tendons, that frequently cause local soreness and referred pain. Although it may not be possible to agree with the author that the cause of localized tenderness and referred pain is mainly relaxation of ligaments, the treatment he advocates is logical for many of the conditions that produce backache with referred pain. Many orthopedists have found the use of a local anesthetic for the injection of "trigger points," with or without the added injection of other substances such as hydrocortisone or a mild irritant, to be helpful in relieving this painful syndrome. This is an interesting and challenging book, but some of the statements found in it will not be accepted by most orthopedists. The report of such a high incidence of recovery of the patients treated by the author should cause all physicians whose minds are not closed to new ideas to study the methods used and put them to the therapeutic test.

Ciba Foundation Colloquia on Endocrinology. Volume 9: Internal Secretions of the Pancreas. Editors for Ciba Foundation: G. E. W. Wolstenholme, O.B.E., M.A., M.B., and Cecilia M. O'Connor, B.Sc. Cloth. $7. Pp. 292, with 100 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; J. & A. Churchill, Ltd., 104 Gloucester Pl., Portman Sq., London, W.1, England, 1956.

The present colloquium is a follow-up of a previous one dealing with carbohydrate metabolism that was held by the Ciba Foundation in 1952. A group of American and European workers reviewed their recent experimental studies in this field. Their reports as well as the discussions that followed each report summarize most of the research that is now being conducted. The subjects treated are the effects of agents that specifically alter the alpha cells of the pancreas, glucagon, the chemical structure and configuration of insulin, the permeability of cells to glucose and other sugars, the hepatic actions of insulin, and the interactions of pituitary growth hormone and insulin in the organism. Since the book deals primarily with animal experiments, it will be of primary interest to the research worker rather than to the clinician. The demonstration, however, that destruction of the islet tissue affects carbohydrate metabolism quite differently than does pancreatectomy and the observed actions of the hyperglycemic glycogenolytic factor of the alpha cells may alter radically our present notions of the pancreas and carbohydrate metabolism and may have practical clinical significance. As with the other volumes in this series, the editors and publishers have produced a well-written and excellently printed book.

Fluid Balance Handbook for Practitioners. By William D. Snively, Jr., M.D., *Attending Physician, Evansville Child Health Clinics,* and Michael J. Sweeney, M.D., Attending Physician, Evansville Child Health Clinics, Evansville, Ind. Cloth. $6.75. Pp. 326, with illustrations by Kathleen Calhoun. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, *England; Ryerson Press,* 299 Queen St., W., Toronto 2B, Canada, 1956.

This is an exceedingly well-written book by two authors who are well qualified to discuss this subject. They have presented all the problems of fluid imbalance in a simple logical fashion. The types and composition of body fluids and their shifts are specifically discussed. Electrolyte imbalance and all the clinical problems of acid-base equilibrium are included, and the methods of handling these problems are discussed. Specific instructions for determining amounts, kind, and rate of fluids are suggested by a simple set of rules. There are actual case problems presented at the end of the book as exercises for handling specific imbalances. This small volume can be read in a few hours. The format is pleasing, and the illustrations, figures, and tables are excellent. The bibliography is rather scant. This book can be recommended to all students and to practioners of medicine and surgery who are confronted with problems of fluid imbalance.

Textbook of Urology. By Victor F. Marshall, M.D., F.A.C.S., Associate Professor of Clinical Surgery (Urology), Cornell University Medical College, New York City. Cloth. $5.50. *Pp.* 268, with 66 illustrations. Paul B. Hoeber, Inc. (*medical book department of* Harper & Brothers), *49 E. 33rd* St., New York 16, 1956.

This book represents a needed concise, accurate urologic textbook. The contents are well arranged and presented in a straightforward manner. The urologic concepts are those current in the field of diagnosis and treatment. The diagrammatic representation of urologic disease as a pyramid leading to a cure is clever. The base of that pyramid is an adequate history and physical examination, tools available to all interested physicians. The text reads easily and is occasionally interspersed with appropriate comments. This book is recommended for medical students and practicing physicians.

QUERIES AND MINOR NOTES

LIGHTNING PAINS

To the Editor:—*A 42-year-old man contracted syphilis in 1938, after which he had a course of treatment of bismuth and mercury. This course was completed in 1944, and since then he has had penicillin ranging up to 6 million units. The primary symptom at present is apparently that of a neuritic pain largely involving the knees. X-ray revealed no evidence of syphilitic involvement, and neurological examination is negative. He has a persistently positive reaction to the Wassermann, Mazzini, and Venereal Disease Research Laboratory tests. The pain this man is experiencing can be dulled with aspirin, Empirin, or Demerol, but not completely relieved. Otherwise he is in good health and is able to work in the oil fields regularly. What course of treatment might be available for prevention of the pain or at least a check of its frequency?*

M.D., Montana.

Answer.—The information provided is inadequate to permit an opinion as to whether the neuritic pain primarily involving the knees is or is not potentially associated with the patient's long-standing syphilitic infection. So-called neuritic pains in patients with late syphilis are practically always characteristically lightning or lancinating in character. The character of the pain is sharp, stabbing, and knife-like, each individual pain lasting only for a second or a fraction thereof. These pains tend usually to occur in the lower extremities and are characterized by the fact that they shift from one place to another, sometimes in a toe or sometimes in the ankle, the calf, the knee, or the thigh. They tend to occur in attacks of varying severity, ranging from minor inconvenience that is readily relieved by a mild analgesic, such as aspirin, up to attacks of agonizing severity that may require large doses of morphine or other powerful analgesics. The individual attack of pain may last for an hour or two only or may continue for days at a time. In most cases, the attack ceases either spontaneously or after administration of analgesic drugs, and the patient is completely free from discomfort in the interval between the attacks. This interval may vary from days or weeks to months. An extraordinary feature of this type of pain is that the attacks may be precipitated or triggered by several widely varied circumstances, including a change in the weather, an elevation of body temperature, the presence of focal infection, fatigue—whether physical or mental—and constipation. The attacks are only occasionally completely relieved by any form of antisyphilitic therapy, whether metal or antibiotic chemotherapy, though some patients may obtain partial relief in terms of lessened frequency and severity of attacks.

The diagnosis of lightning pains depends entirely on the patient's description of his subjective discomfort, plus, in most cases, associated neurological evidence of tabes dorsalis. The pains are due to involvement of the posterior roots and columns of the spinal cord and may constitute the earliest symptom of tabes, appearing before there are objective evidences of neurological damage. Pains of this nature do not occur in any other condition. If the patient's pain is of the nature described, it seems reasonably certain that it is due to the old syphilitic infection and that confirmation of this may be had either by very careful neurological examination, with particular reference to objective evidence of damage to posterior columns of the spinal cord, and/or by examination of the cerebrospinal fluid, which does not appear to have been done. The management and treatment of lightning pains often call for the highest skill in the art of medicine, with many ancillary factors to be considered other than antisyphilitic treatment itself. In this particular patient, if the neuritic pain does not conform to the description given above, it is highly improbable that these pains have anything to do with syphilis.

TOXICITY OF 2,4-DICHLOROPHENOXYACETIC ACID (WEED SPRAY)

To the Editor:—*A farmer who has been perfectly well began using 2,4-dichlorophenoxyacetic acid (2,4-D) to spray weeds several weeks ago. He inhaled considerable spray, after which he had a burning sensation in the throat and chest, became weak, and lost his appetite and some weight. Examination of the urine revealed nothing except 2+ albumin, with no casts or blood cells. On discontinuing use of the spray, he gradually improved and the urine has cleared up. This trouble came on also last year and the year before when he used the same spray. On two occasions, he had two other men helping him, both of whom became ill in a similar manner, requiring several weeks for recovery. In the July 18, 1953, issue of* The Journal, *page 1144, the following statement appeared in an editorial "Relief from Ragweed": "2,4-D is comparatively harmless to animals and humans." The article also states that "the dusts of 2,4-D can be irritating to the eyes and respiratory tract," but no reactions were mentioned that were as severe as apparently occurred in these people. Could this illness be due to inhalation of 2,4-D?*

W. E. Wilson, M.D., Northfield, Minn.

Answer.—All available evidence tends to indicate that the sodium salt of 2,4-D is relatively nontoxic when wet or dry clouds are inhaled. Animal experiments with this material did not produce any evidence of lung irritation; however, in concentrated form it is likely to be irritating. The oral $L. D._{50}$ for mice is about 280 mg. per kilogram. Injection of 150 to 200 mg. per kilogram produced myotonia followed by sluggishness and shallow respiration in mice. There is a possibility of individual sensitivity to 2,4-D in persons susceptible to phenol compounds; 2,4-D formulations contain petroleum distillates that may cause varying degrees of discomfort. This factor should be taken into consideration in complaints after exposure to this class of herbicides.

SIDE-EFFECTS OF RADIOTHERAPY

To the Editor:—*Has the value of nicotinamide been scientifically demonstrated for the prevention of the side-effects of radiotherapy? In the city, most of the radiologists routinely prescribe liver extracts and/or vitamin B_{12} for patients exposed to x-rays to prevent postradiotherapeutic leukopenia and anemia. This practice seems illogical, particularly in leukemias and allied disorders, because well-conducted radiotherapy is likely to relieve a preexisting anemia and not aggravate it and these substances probably further the development of the leukemic cells. Are these assumptions correct? What about the use of glutathione, cysteine, thymonucleic acid, and cortisone to prevent the side-effect of radiotherapy?*

Jacques Messerschmitt, M.D., Algiers, Algeria.

Answer.—There are two categories of side-effects of radiotherapy to be considered: First, nausea, vomiting, and malaise after treatment and, second, leukopenia and depression of platelets and eventual anemia. In the first category, derivatives of vitamin B complex, such as nicotinamide or nicotinic acid, with or without pyridoxine hydrochloride, have been helpful on clinical trial. Gravidox, which is a mixture of 20 mg. of pyridoxine hydrochloride and 20 mg. of thiamine hydrochloride, three tablets three times a day, may be helpful. In regard to the second category, leukopenia and depression of platelets may follow total body irradiation or treatment over large areas of the body as commonly given for lymphomas and leukemias. There is no reason for routine administration of liver extract and vitamin B_{12} for this difficulty. Small doses of cortisone acetate, usually 25 mg. given twice daily, until the white blood cell count returns to normal, may be helpful in many cases. Many experiments with animals have been reported using glutathione and cysteine after heavy doses of total body irradiation, but it is not believed that these substances have been used to any extent clinically.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

POSTNASAL TAMPON FOR NASAL HEMORRHAGE

To THE EDITOR:—*Is there information available on the origin of the routine postnasal pack used for nasal hemorrhage?*

Ernest E. Alvin, M.D., San Francisco.

ANSWER.—A brief mention of the postnasal tampon technique was given by Philipp Scheck in 1884. The historical documentation of this procedure is not so simple, as it means ferreting out of a case description of such a technique that might be so identified. Priority is lost in antiquity and may not be well established, but one of the best descriptions was offered by P. McBride in his "Diseases of the Throat, Nose and Ear" (ed. 2, Philadelphia, P. Blakiston's Son and Company, 1894, pp. 272 and 273). It follows: "If it is desired to plug the posterior nares a small-sized, soft rubber catheter is the best instrument to employ. To its extremity is attached a string of sufficient length. The point is now passed into the nostril, while the patient sits, with open mouth and light thrown on the pharynx, before the surgeon. When the latter sees the catheter appear below the palate he seizes it with dressing forceps, and pulls it and the attached string out through the mouth. A pledget of lint, preferably saturated with vaseline, to which some antiseptic has been added, if there be a prospect of the plug having to remain *in situ* for any length of time—is now attached to the string about 18 inches from its extremity, and pulled up behind the palate, after which the two projecting strings are tied together. It is often useful at this juncture, to introduce the finger to guide the pledget past the uvula and soft palate. If it be only desired to plug the anterior nares, a long strip of lint—saturated with vaseline to prevent sticking—is pushed in by dressing forceps. Plugs produced by distending membranous or india rubber bags, with air or fluid, have been employed, but they seem only complicated methods of arriving at the same result."

INSECTICIDAL FOGGING OF HOSPITAL GROUNDS

To THE EDITOR:—*We purchased an insecticidal fogging machine in an endeavor to control mosquitoes and flies in the vicinity of the hospital grounds. The active ingredients in the insecticide used are chlorophenothane, 8%; isobornyl thiocyanoacetate, 1.55%; related terpenes, 0.45%; and petroleum distillate, 92.5%. Please advise as to the danger, if any, to human and plant life and, also, as to the precautions to be taken and/or substitutes to be used in the fogging procedure to rid the area of mosquitoes and flies.*

Louis J. Ptacek, M.D., Oconomowoc, Wis.

ANSWER.—If the fogging is done by responsible and trained persons acquainted with the dispersal of such preparations, it is rather unlikely that members of the hospital community would be exposed to dangerous amounts of the material from either acute or chronic toxicity viewpoints. Contamination of fruit or vegetables in gardens or in the hospital is equally unlikely because of the nature of the dispersal and the small quantities of the insecticidal materials used. Persons suffering from asthma or hay fever might experience respiratory difficulty if they were in immediate contact with the fog. Fogging operations, however, are usually conducted after sundown, or later in the evening, and at distances of 25 to 50 ft. from the nearest dwellings. The nature of the dispersal and the meteorologic conditions for successful fogging operations are such that gross exposure to fogs by such persons can be readily avoided. Wildlife is reported to be not injured when large areas of forest are fogged with chlorophenothane. Birds, bees, butterflies, and other forms of beneficial life commonly seen around residential areas are also probably safe for the same reasons.

TREATMENT OF HYPERPIGMENTATION

To THE EDITOR:—*I would like information regarding the use of monobenzyl ether of hydroquinone in the treatment of hyperpigmentation of the skin.*

E. G. Kettelkamp, M.D., Monona, Iowa.

ANSWER.—Monobenzyl ether of hydroquinone (MBH) is the only known chemical agent that inhibits the formation of melanin pigment when applied to the skin. Other drugs, including the so-called bleach creams, bring about an apparent decrease in skin pigmentation by exfoliation of the outer pigmented horney layer. Although MBH is an effective topical agent for decreasing melanin pigmentation, it has several major disadvantages: 1. About 13% of patients develop a contact dermatitis. 2. The decrease in pigmentation is very slow, requiring six to nine months in some patients. 3. The resulting depigmentation is often not uniform but mottled, especially in the Oriental and Negroid races. 4. For some unknown reason MBH is effective in only a relatively small percentage of patients treated. The use of MBH should therefore be limited to disfiguring melanin hyperpigmentation in the Caucasian race. If no effect is noted after 9 to 12 months of application, therapy should be discontinued. MBH, being an inhibitor of melanin formation, has no effect on pigmentation resulting from iron, silver, or artificial pigments. A commercially available ointment contains 20% MBH in a washable base.

FISH POISONING

To THE EDITOR:—*A patient in Havana, Cuba, had an acute episode of diarrhea lasting seven days. He claimed to have eaten fresh broiled barracuda meat, which he caught himself. Even though the barracuda is a man-eating fish, is there any special reason why this type of fish poisoning is different from other fish or shellfish poisoning?*

C. D. J. Generales, M.D., New York.

ANSWER.—Fish poisoning resulting from the ingestion of fresh (unspoiled) barracuda is generally classed under the syndrome known in the Caribbean area as ciguatera. More than 300 species of fish have been reported as being capable of producing ciguatera-like symptoms. Prolonged diarrhea is a common component of this complex. The only relationship between the barracuda's man-eating tendencies and its toxicity is its size, i. e., only the larger specimens are likely to be dangerous. Shellfish poisoning is caused by a toxic substance found in certain marine protozoa (dinoflagellates), on which the shellfish inadvertently concentrate for food during certain seasons of the year. The poisonous substance that produces shellfish intoxication is not the same as that which produces ciguatera-like symptoms.

BCG VACCINATION

To THE EDITOR:—*May I point out in answer to the query entitled "Exposure of Children to Tuberculous Grandmother" (J. A. M. A. 161:926 [June 30] 1956) that I would recommend BCG vaccination if the grandchildren have a negative reaction to the tuberculin test. Six to eight weeks after vaccination, if the children's reactions to the tuberculin test have become positive, let them visit the grandmother, who I assume is receiving antimicrobial treatment. I would have the grandmother as well as the children take the accepted precautions against infectious disease. This advice is based on my long experience, both in the laboratory and in the field, with the use of attenuated, viable tubercle bacilli as immunizing agents against tuberculosis and is supported by the experiences of other investigators. The consultant's answer has become practically a slogan for those who have had little experience with immunizing agents in tuberculosis and has also been used by opponents of other forms of vaccination and treatment. It would be of interest to readers of* THE JOURNAL, *and to those of us engaged in the study of immunization against tuberculosis, if the consultant would present the statistical data on which he bases his statements and compare them with the data of Ferguson, Rosenthal, the Medical Research Council, myself, and others who have evaluated BCG vaccine under control conditions.*

In support of my own views, may I summarize a study, which was initiated in 1936 and which culminated in 1956, to determine under field conditions the value of BCG vaccine. A group of 1,551 children of preschool and school age who had negative reactions to the tuberculin test received an intracutaneous injection of BCG vaccine and were not revaccinated. A group of 1,457 children of comparable age and sex who had negative reactions to the tuberculin test received an intracutaneous injection of saline solution and served as controls. An analysis of 26,580 roentgenograms of the chest taken annually for the first 9 to 11 years of this study showed that 4.1% of the vaccinated and 16.4% of the control patients showed *tuberculous lesions—0.7% miliary in nature, none among the vaccinated; 12.5% and 14.8% of the vaccinated and control patients, respectively, showed nontuberculous lesions. An appraisal of the protective value of BCG vaccine, 15 years after the initiation of the same study, was published in* THE JOURNAL *(149:334 [May 24] 1952) by C. F. Aronson and me. At that time, 12 of the vaccinated and 65 of the control patients had died of tuberculosis while 59 and 63 of the vaccinated and control patients, respectively, had died from nontuberculous causes. Of the 65 deaths from tuberculosis, 19 had been due to miliary tuberculosis. None of the vaccinated patients had died from this form of tuberculosis.*

In 1956, 18 to 20 years after the initiation of the study, we again determined the mortality from all causes and from tuberculosis among the 3,007 persons in the study, and traced all but 24 persons. At this time we found that 13 of the vaccinated and 68 of the control patients had died from tuberculosis, 45 of the vaccinated and 42 of the control patients had died from nontuberculous diseases, and 44 of the vaccinated and 40 of the control patients had died from the results of violence.

The preliminary report of the Medical Research Council, published in the British Medical Journal, *Feb. 25, 1956, shows that among over 50,000 adolescents followed in this study the annual incidence of tuberculosis was 0.37 per 1,000, compared with 1.94 per 1,000 among the control patients. Will the consultant cite any reference indicating that multiple cases of tuberculosis have followed the use of BCG vaccine from one laboratory or from one lot of vaccine?*

Joseph D. Aronson, M.D.
Henry Phipps Institute
Philadelphia.

For additional discussion of this subject, see THE JOURNAL, Oct. 13, 1956, pages 698-700.—ED.

RESEARCH REVIEWS

From time to time there will be published in this section of THE JOURNAL *brief but not necessarily complete reviews of some of the newer clinical aspects of medical research and practice. This material is gathered specifically for* THE JOURNAL.—ED.

NONSPECIFIC DEFENSE MECHANISMS OF THE BODY

Current interest in the study of natural resistance to infection found expression at a conference of the New York Academy of Sciences, Section of Biology, in New York. The mechanisms of "general resistance" are being unraveled gradually. There are several independent defense systems by which the body guards against invading bacteria, viruses, and protozoa. Some of these mechanisms have been defined recently.

The Properdin System.—The recognized components of the properdin system are properdin, complement, and magnesium ions.[1] According to its discoverer, L. Pillemer,[2] Western Reserve University, Cleveland, properdin is a euglobulin that contains lipid, carbohydrate, and phosphorus. It is normally always present in the serum of man and mammals without previous antigenic stimulation. Serum from rats reared under sterile conditions contains a normal amount of properdin. Properdin is not an antibody. Its action is nonspecific. To become active, properdin requires complement (C′) and magnesium ions.

While it was thought in the past that the presence of antibody is necessary for the action of complement, the discovery of the properdin system has demonstrated that complement also plays a part in bactericidal defense mechanisms that act in the absence of specific antibodies. Four components of complement have been identified: C′1, C′2, C′3, and C′4. All four components are essential in the properdin system. To kill gram-negative bacteria, for instance, C′1, C′2, C′3, C′4 and magnesium ions must be present.

Magnesium in the properdin system cannot be replaced by sodium or calcium. Under experimental conditions—and only in unphysiologically high concentrations—cobalt or manganese may replace magnesium. Thus, under normal circumstances, magnesium plays an essential part in the body's natural defense against infection.

Normal human serum contains 4-8 units of properdin per milliliter, rat and mouse serum 25-50 units, and guinea pig serum less than 3 units. One may speculate whether these species variations reflect differences in natural resistance to infection. Stray dogs have a properdin level that varies from the normal for dogs of 12 to 18 units per milliliter to near 0. In some areas, especially in the South, stray dogs have an almost uniformly low titer. If they are given proper care and good food, their titer can be restored to a normal level.

In normal individuals the properdin level remains constant. It bears no relation to age or sex. L. Pillemer[3] and C. F. Hinz Jr. and J. R. Murphy,[4] Western Reserve University, Cleveland, have reported that fever, variations in the leukocyte count, and some other factors do not influence the properdin level. In patients with infections due to gram-negative bacteria, pneumococci pneumonia, and paroxysmal nocturnal hemoglobinuria, it has been found that the properdin level is low.

In vitro, the properdin system present in normal human serum destroys bacteria, inactivates viruses, kills protozoa, and lyses abnormal erythrocytes. In experimental animals, there appears to be a relation between the serum properdin level and shock, susceptibility to bacterial invasion after irradiation, and resistance to infection in general.

J. Fine, Harvard Medical School, Boston, and his collaborators have found that hemorrhagic shock in dogs reduces the serum properdin level considerably, while there is no change in the total and differential leukocyte count or in the hemolytic activity of complement in vitro.[5]

O. A. Ross,[6] Western Reserve University, Cleveland, has reported that total body irradiation of mice results in a profound drop in the properdin level and fatal bacteremia. The effects of the administration of properdin under these circumstances have been studied. When properdin is given during the postirradiation period, it partially protects the animals and prevents death. When it is given too early, it does not prevent the onset of bacteremia. Pillemer believes that it may be dangerous to give properdin at the height of bacteremia, since its bactericidal action may release such an overwhelming amount of endotoxin at one time as to cause toxic shock and death.

The bactericidal action of the properdin system has been demonstrated.[7] When bacteria invade the blood stream they are attacked immediately. This is a nonspecific effect. Specific antibodies in response to antigen stimulation are only formed after several days. The properdin system thus forms the first defense. Its action is supplemented by the formation of antibodies that deal with the surviving bacteria.

According to D. Rowley,[8] St. Mary's Hospital, London, England, the lipopolysaccharide fraction in bacterial cell walls may be the substrate for the serum bactericidal reaction. He found that following the injection of cell walls of various gram-negative bacteria there were changes in nonspecific immunity to experimental infection with Escherichia coli and Salmonella typhosa. In addition to these organisms, M. Landy,[9] Army Medical Service Graduate School, Washington, D. C., has shown that injection of lipopolysaccharides into mice also causes a transient increase in nonspecific resistance to experimental infection with Proteus vulgaris and Pseudomonas aeruginosa. This increase in resistance following bacterial lipopolysaccharide injection is accompanied by elevated properdin titers.[10]

Highly purified lipopolysaccharides have been prepared.[11] Lipopolysaccharide from Salmonella abortivoequina is a powerful pyrogen, and its effects when injected into man have been studied.[12] The question yet to be answered is whether injection of such lipopolysaccharides prepared commercially offers a practical way of raising the properdin level clinically.

Fresh normal serum inactivates influenza A and B, mumps, Newcastle disease, and vaccinia viruses; in conjunction with antibody, it also inactivates Rous sarcoma, Western equine encephalomyelitis, herpes simplex, and dengue viruses. It is inactive against poliomyelitis and the recently described adenoviruses. H. S. Ginsberg and R. J. Wedgwood,[13] Western Reserve University, Cleveland, have shown that the properdin system inactivates the virus of Newcastle disease. There is no evidence yet as to the role that the properdin system may play in natural or acquired immunity to viral infection in man. The heat-labile component of normal serum reported in 1949, which neutralizes virus infectivity and inhibits hemagglutination,[14] is probably identical with properdin.[1]

Also, the heat-labile serum components and magnesium required for toxoplasma antibody to exert its adverse effect upon the parasite may be identical with the properdin system, according to H. A. Feldman,[15] State University of New York, Syracuse, and other workers.[16]

Recent studies in man [17] indicate that various types of anesthesia, elective surgery, accidental trauma, adrenalectomy, and removal of the spleen do not cause significant changes in the serum properdin titer. The properdin level has been found to be depressed in certain surgical cases in association with peritonitis, pneumonitis, atelectasis, paralytic ileus, gastrointestinal hemorrhage, and wound infection following burns. In a few patients subjected to extreme variations in corticosteroid maintenance therapy after adrenalectomy, no significant changes in serum properdin titer were noted.

At present, properdin is not available for clinical use. Two ways of increasing the amount of naturally occurring properdin are being considered: (1) the injection of lipopolysaccharides and (2) the fractionation of plasma.

Little is known yet about the practicability of the first method. The second method is under intensive study in Boston. Since the preparation of properdin from serum presents a number of difficulties, plasma from blood collected over an exchange resin is being used. Initial laboratory production promises a yield of about 1 million units of purified properdin per year. With pilot plant production, it should be possible to increase this yield to about 6 million units per year, and with other measures now contemplated perhaps to more.

Before properdin can be made available for clinical use, problems of sterility, stability, and freedom from pyrogenic and other untoward effects must be solved. J. Fine estimates that an adult depleted of properdin may require a therapeutic dose of as much as 10,000 to 20,000 units; hence the amount for clinical investigation that may be expected for the time being will be very little indeed.

Other Defense Mechanisms.—J. L. Tullis and D. M. Surgenor,[18] Harvard Medical School, Boston, have reported the isolation of two new proteins that control the ability of leukocytes to ingest bacteria. They were isolated from plasma. One is a betaglobulin; the other, an alpha-1 globulin. They are different in their chemical behavior, but similar in their physiological activity of promoting phagocytosis. They have been called phagocytosis-promotion factors. Purified preparations of properdin have no phagocyte-stimulating effect.

J. G. Hirsch,[19] the Rockefeller Institute for Medical Research, New York, has investigated the mechanism that leads to intracellular death of engulfed micro-organisms. He believes that lysozyme present in polymorphonuclear leukocytes does not account for the bactericidal power of these cells, since many micro-organisms insusceptible to lysozyme are killed in phagocytic cytoplasm. He has isolated a specific protein from the cytoplasm of polymorphonuclear leukocytes, which is thought to be responsible for the bactericidal action. The name phagocytin has been proposed for this protein. Its enzyme type of action is different from that of previously known antibacterial agents derived from tissues.

The study of these and other factors that may play a role in the natural defense mechanisms of the body is being actively pursued.

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« Washington News »

Military Dependent Medical Care Program Starts • •
FDA Administrator Again Denounces Hoxsey Clinics • •
State-by-State Study of Higher Education Urged • •
Plans for Hearings on Medical Education Dropped • •

MILITARY DEPENDENT MEDICAL CARE

On December 7, the Defense Department inaugurates a large new medical care program, designed to give uniform benefits outside military medical facilities to perhaps as many as 1 million wives and children of members of the uniformed services. Army Surgeon General Hays describes it as "the beginning of a new era in medical care and one that may set a new pattern in cooperation between civilian and military medicine."

At the outset at least, all wives and children will have freedom of choice between military and private facilities. If their choice is the latter, the new program provides that the federal government will pay most of the expense of hospitalization and preoperative and postoperative services. In civilian facilities, outpatient service is strictly limited. If, after a period of trial, the Secretary of Defense finds that military medical facilities are not used sufficiently, he may restrict private care in certain areas.

In military facilities, dependents will pay $1.75 per day. In private facilities, they will be charged the same fee or a total of $25, whichever is the larger. Other expenses will be met by the government. Financial arrangements will be handled by Blue Cross and commercial insurance companies for the private hospital phase. The medical care phases will be handled by arrangements worked out on a state-by-state basis by state medical societies and the Department of the Army, which is agent for the Defense Department in administering the program. Some societies are handling the medical care bookkeeping themselves, while others have entrusted it to Blue Shield or other organizations.

Dependent parents and parents-in-law of members of the uniformed services will be entitled to care on a space-available basis in military facilities but are not covered by the civilian program. In addition to the Army, Navy, and Air Force, the new program also includes dependents of members of the Coast and Geodetic Survey, the Coast Guard, and the commissioned corps of the U. S. Public Health Service.

In explaining the program's objectives shortly before the starting date, General Hays emphasized that the most important feature was the provision of medical care to service families "who heretofore could not avail themselves of medical service in uniformed facilities because of distance and overtaxed facilities." He added: "Until operating experience is gained, no firm evaluation of the impact of the program on the uniformed medical services can be made. At the present time, however, significant changes in personnel and bed requirements do not appear likely."

He said that, if the program produces the results hoped for, "it should be important in promoting career service to a greater percentage of our forces. If only a small percentage of the one million men we lose annually can be retained through the provisions of this legislation, then it will pay for itself many times over."

From the Washington Office of the American Medical Association.

HOXSEY CANCER REMEDY

Following upon a federal court condemnation of the Hoxsey medicines as "illegally offered as an effective treatment for cancer," the U. S. Food and Drug Administration warns all cancer patients and their families that "this action does not end the meances of this fake treatment." A statement by FDA Administrator George P. Larrick reviews the action of the Pittsburgh court, stating that this "merely means that half a million of the Hoxsey pills, which were seized shortly after the opening of a second Hoxsey Clinic at Portage, Pa., will now be destroyed." The FDA will seek an injunction to stop further interstate shipment of the pills. Adds Mr. Larrick: "We intend to use every legal means within our power to protect consumers from being victimized by this worthless treatment."

The statment says that it is "of the utmost importance" that cancer patients and their families who may be planning to employ the treatment at the Hoxsey clinics at Dallas, Texas, or Portage, Pa., should acquaint themselves with all the facts. They are advised to write the Food and Drug Administration in Washington for a copy of a public warning issued by the FDA last April.

The FDA statement continues: "Harry M. Hoxsey has continued to promote his worthless cure for more than 30 years, notwithstanding numerous local and state court actions. Proceedings under the Federal Food, Drug, and Cosmetic Act did not appear possible until a 1948 decision of the Supreme Court interpreting the word 'accompanying' in the definition of labeling under the Act. An injunction suit was field in 1950 and a decree finally issued by the Federal court at Dallas in 1953. Over the years thousands of persons have been deceived by the false claims for the Hoxsey liquid medicines and pills. At the Pittsburgh trial there was testimony concerning persons who may have died of cancer as a result of reliance on the Hoxsey treatment instead of seeking competent medical treatment in the early stages of their condition. The Government's evidence showed that alleged 'cured cases' presented by defense attorneys were people who did not have cancer, or who were adequately treated before they went to the Portage clinic, or died of cancer after they had been treated there."

GOVERNMENT-FINANCED STUDIES

A state-by-state analysis of higher education needs for the next 20 years, with the possibility of the federal government helping finance the studies, is proposed in the first interim report of the President's Committee on Education Beyond the High School. The report declares: "Even while the localized needs are thus being specified and defined by the state studies, consideration must be given to how and by whom . . . the increasing costs of supporting more individual students, training more teachers and building more buildings shall be borne. It is already clear that present resources will be grossly inadequate."

(Continued on page 22)

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Washington News—Continued

The committee said it will "weigh proposals for grants for teacher training, loans for other than self-liquidating buildings, grants for various kinds of physical facilities, construction of ROTC facilities at federal expense, and still other proposals that are already being considered by some legislators."

It scored the lack of any over-all educational policy, in the face of the fact that the federal government in recent years has spent more than a billion dollars in the field of education beyond the high school. "Over and above these separate programs, the federal government is now being called upon for an increasing number of other forms of support such as extension of loan programs, scholarship aids, especially for aspiring teachers, special 'crash programs' for production of doctors and even contributions toward vocational training. . . . The federal government has no clear and explicit policy to guide the consideration of such proposals."

The report also warned that the "inflexibility of the prevailing pattern of 12 years in elementary and secondary schools, four years in college and two, three or more years in professional school" was in conflict with contemporary social trends. "It fails to account for the varying aptitudes of students and for the cumulative effect upon their lives of the lengthening curriculum when coupled with existing obligations, earlier marriage ages and earlier retirement ages."

In expanding and diversifying opportunities or speeding up the formal educational process, the committee stressed, "we must never lose sight of the crucial importance of maintaining high standards, and we must be constantly alert to improve the quality of the educational offerings."

MEDICAL HEARINGS

Plans for a series of panel-type hearings on problems and needs in medical education originally set for this fall have been given up by the House Interstate and Foreign Commerce Committee. Changes in the make-up of the committee, including the death of Chairman Percy Priest, have forced abandonment of the hearings, at least for this year. Decision on whether to go ahead with a study of this type next session will hinge on the new chairman, Rep. Oren Harris (D., Ark.), and the reconstituted committee. The committee staff, meanwhile, is continuing to gather material on the financial needs of medical schools, and the supply and demand of medical school applicants, as directed by the committee just before the 84th Congress ended.

During debate last session on the bill for federal grants to help schools and other research centers build laboratory facilities, efforts were made on the House floor to broaden the measure to include money for classrooms. Congress decided instead that this subject needed more study. Original plans for the Interstate Committee hearings called for witnesses representing the professions, the medical schools, and various groups utilizing doctors' services to appear on a series of panels. The panel approach to legislation was used several years ago by former Chairman Charles Wolverton (R., N. J.), in investigation into broad health problems and again on the Salk poliomyelitis vaccine situation.

MEDICINE'S FUTURE

"Whether there is further government intervention in the field of medicine will depend largely upon medicine's willingness to carry the torch of free enterprise for the private practice of medicine," Dr. David Allman, President-Elect of the American Medical Association, told delegates to the Southern Medical Association convention, meeting in Washington, D. C.

The association's four-day golden anniversary meeting was attended by more than 5,000 physicians and guests. Dr. Allman's speech, at the last general session, was part of a program that included presentation of over 300 scientific papers and a symposium on industrial health. Panel members included Dr. Elmer Hess, past-president of the A. M. A., and Bradshaw Mintener, former Assistant Secretary of the Department of Health, Education, and Welfare.

Dr. Allman, in his address entitled "Who's Going to Carry the Torch," pointed out, "Today the threat of government intervention in medical affairs and in the relationship of doctor and patient is more imminent than ever before." He then stressed, "Our first responsibility is still to provide good medicine and good service to our patients at home. If we do this, we will be held in high regard by the people we serve. Then, and only then, will our chances of success on the political front be improved." At this general session, Dr. J. P. Culpepper Jr. of Hattiesburg, Miss., was installed as the new president. He succeeds Dr. W. Raymond McKenzie of Baltimore.

MISCELLANY

An estimated 2.4 billion dollars, a 7% increase over 1955, was spent in the 1956 fiscal year for scientific research and development by the federal government. These statistics are from the report, *Federal Funds for Science*, V, of the National Science Foundation. . . . Gen. Alfred M. Gruenther will begin his term as president of the American Red Cross on Jan. 1. He is retiring as supreme allied commander in Europe. . . . The Federal Civil Defense Administration is augmenting its medical storage program by an emergency supply support program providing "distribution in depth." . . . In the coming year the Influenza Information Center of WHO will be located at the National Office of Vital Statistics. . . . Two Veterans Administration doctors have devised a test that they believe may prevent the fatal hemorrhages of cirrhosis of the liver. Excessive pressure of blood is measured by inserting a hollow needle into the spleen. . . . Water treatment works in 9,000 U. S. cities and towns have been listed by the Public Health Service as in need of repair. This is one step in a new program of federal grants to help in constructing water treatment works. . . . A centralized orthopedic shoes service has been established by the VA. The new system is designed to provide better service to the veterans and to save $50,000 to $60,000. . . . Employees of the VA hospital in Fort Lyon, Colo., will receive an incentive award of $4,360, the largest in the history of the VA. . . . The first phase of a program designed to select and train future executives at all levels has been started by the Veterans Administration. The program, brought about by a possible 49% loss of executives during the next five years through retirement, now pertains only to key officials in the central Washington office and in field stations.

(cont'd)

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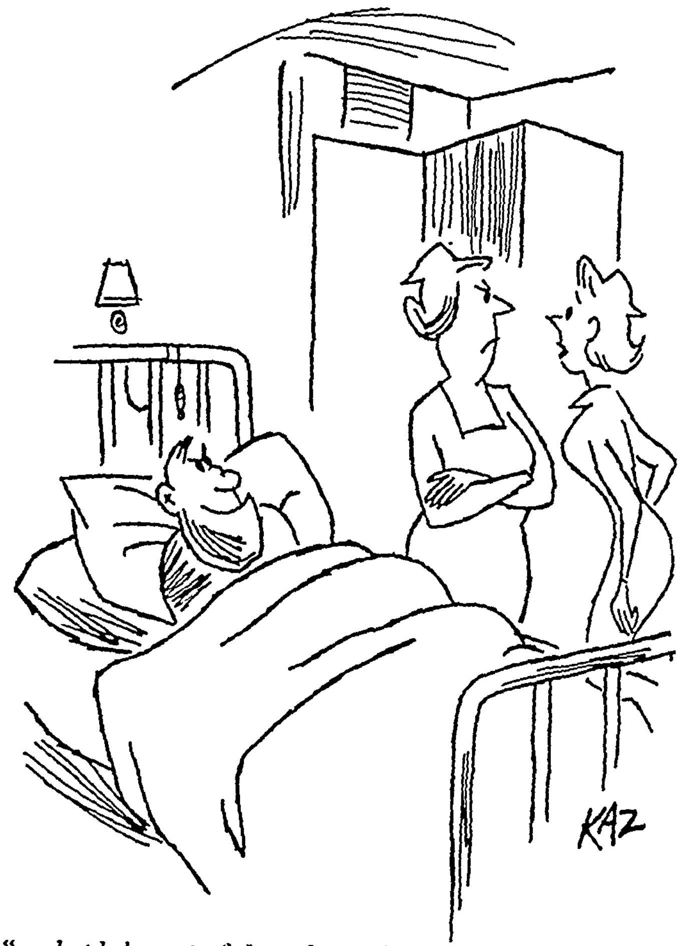

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THE JOURNAL

of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 162, NO. 14 CHICAGO, ILLINOIS DECEMBER 1, 1956

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OCCUPATIONAL DEAFNESS

Meyer S. Fox, M.D., Milwaukee

• *A worker's hearing can be damaged temporarily or permanently by sufficiently loud occupational noise, whether explosive or continuous. Audiograms made before and during the course of employment are essential to a program of conservation of hearing; they are also essential for medicolegal purposes. Medical supervision is important. The physician who is consulted in disputes about cases of allegedly occupational deafness is on safe ground when he confines himself to statements of demonstrated fact and when he avoids suppositions. The otolaryngologist is especially qualified to collect the facts needed to conserve the hearing of workers and to prevent economic loss to employers from ill-founded claims.*

Occupational deafness is assuming increasing importance in our everyday life. Not only does it directly affect the workers and employers but also it concerns other segments of society. As physicians we are primarily interested in the medical and medicolegal aspects of the problem. As otologists we are concerned with the hearing and communication problems. Because of space limitation, it will be impossible to go into any detailed discussion. I shall therefore confine this paper to some personal recommendations and observations that I feel may be of interest and use to the practicing otolaryngologist.

Trauma

Occupational deafness as herein used denotes hearing loss in one or both ears. partial or complete, arising during the course of, or as the result of, one's employment. It may occur suddenly, as the result of traumatic injury, intense blasts, or explosions, or gradually, as the result of prolonged exposure to hazardous noise levels. Direct trauma to the ear usually results from blows, foreign objects, and burns due to sparks and molten metal. The local trauma to the area may be followed by perforation of the tympanum and infection and often is associated with a hearing loss of the conductive or mixed type. These injuries are usually unilateral and tend to heal with proper management. It has been my experience that burns of the ear canal and perforations of the tympanum due to sparks and molten metal are much more common than one would gather from current literature on the subject. Direct blows to the head can result in a hearing loss due to nerve damage, functional hearing tests revealing audiograms similar to those found in noise deafness.[1]

The term *acoustic trauma* is often used to include industrial noise deafness as well as the sudden hearing loss produced by loud noises such as blasts, explosions, and gunfire. Davis,[2] however, feels that the two conditions would better be described by separate terms, in order that one may logically distinguish between them. He therefore uses the term acoustic trauma to mean the immediate injury produced by one or a few exposures to intense sounds, as illustrated by the hearing loss resulting from blasts or explosions. Industrial noise deafness, on the other hand, is used to describe the loss of hearing that develops over a period of months or years of working in an environment of hazardous noise levels.

Noise

Noise has been defined as unwanted sound. It is the result of acoustic waves occurring at random frequencies and intensities. When the normal ear is exposed to noise at damaging intensity levels for a sufficiently long period of time, a temporary depression of hearing results, which disappears after a period of rest. This temporary hearing loss is called "temporary threshold shift." When the ears are exposed for longer periods or to more intense sounds, the hearing loss becomes more severe and the recovery is incomplete. That portion of hearing that never returns is referred to as *noise deafness.*

What are the effects of noise? We know definitely that noise can and does cause loss of hearing and that it interferes with communication. These are referred to as the auditory effects. The nonauditory effects of ordinary industrial noise are, in my opinion, vague and indefinite, the symptoms depending a great deal upon the personal motivation of the worker.

Read before the Section on Laryngology, Otology and Rhinology at the 105th Annual Meeting of the American Medical Association, Chicago, June 13, 1956.

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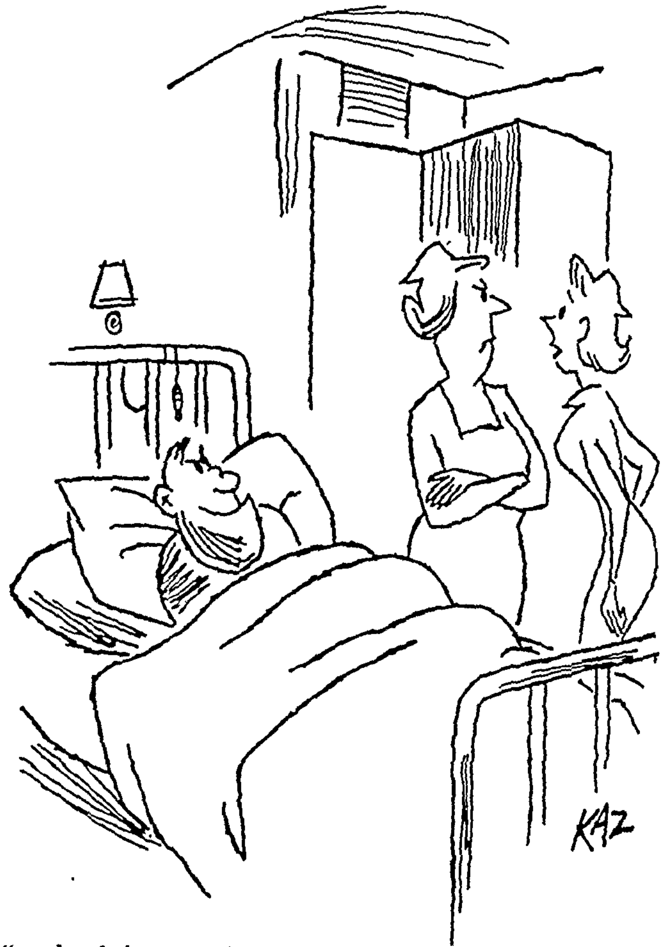

". . . but he's a prizefighter—he won't get up until I count to nine."

"I'm a real he-man, ya' hear me! The doctor said I had athlete's foot!"

compensation laws concerning noise deafness. These questions are gradually being answered by authorative decisions of the higher courts of the various states.[4]

In reviewing the medicolegal problems, it is my opinion that the chief cause for dispute arises from the fact that there were no reliable records that could be used as a base line to determine the worker's hearing at the beginning of employment and during the course of employment. Another important controversial medicolegal development is that pertaining to the various methods for determining hearing loss and for converting this hearing loss in terms of percentage of hearing disability. That there are differences of opinions is established by the fact that various states have different approaches to the same problem. The American Medical Association and the American Academy of Ophthalmology and Otolaryngology recognized the inadequacy of the existing methods of determining hearing disability and a committee of eight persons was appointed to study the problem. After several years of study, this committee published a report on principles for evaluating hearing disability.[5] All otolaryngologists interested in the problem of industrial noise deafness are urged to study this report.

Hearing Conservation Programs

The otolaryngologist, by virtue of his special training, interest, and daily clinical experience with hearing problems, has the qualifications that enable him to be a consultant in the planning and management of industrial hearing conservation programs. In a previous publication[6] I pointed out that the three major objectives of such a problem are to (1) conserve the hearing of workers, (2) avoid unnecessary economic loss to employers, and (3) collect the facts and data in order to facilitate the accomplishment of the two foregoing objectives.

The first requisite of an effective hearing conservation program is a thorough sound survey of the working areas. Such a study is necessary to scientifically determine the frequency characteristics and intensity levels of the noise present in these areas. The information thus gained should indicate whether excessive noise levels are present and, if so, the amount and type of acoustical treatment and individual ear protection that might be required in such working areas. The next step is to obtain a suitable room for the performance of hearing tests. The testing room should be situated in an area that will permit the satisfactory performance of hearing tests without interference due to extraneous noises. In some cases acoustical treatment of existing rooms will result in a satisfactory reduction of the extraneous noises. In other situations acoustical treatment will not bring about the desired result. Where this is not feasible, prefabricated acoustical booths now commercially available provide a satisfactory place for the auditory tests. The personnel who are to do the testing should be sufficiently trained and supervised by the otolaryngologist so that they will develop skill and interest in this work. For the ordinary industrial hearing conservation program, only pure-tone air-conduction audiograms need be taken, and these can be made with a simple, portable, properly calibrated audiometer.

The next phase of the hearing conservation program is the installation of preplacement pure-tone audiometric tests of the workers. This is a must. The preplacement pure-tone audiogram is a base line from which all subsequent studies concerning the worker's hearing status are made. The records that are used should show the audiometric and otological findings and pertinent items of medical and industrial history. All workers exposed to high-intensity noise levels should have periodic checkups of their hearing.

The results of all hearing tests are reviewed and evaluated, and those workers who show significant hearing loss at the beginning of employment or during the course of employment are referred to the otologist for examination and further hearing studies. This procedure results in the establishment of accurate records that can be used for purposes of job-placement and of ear protection and as a base line for future audiometric studies. It also establishes valid records made by a qualified otologist that can be used in the event industrial claims of hearing loss arise at a later date. I am aware of the fact that many industries have purchased audiometers and have turned over the job of testing workers' hearing to health and safety personnel without adequate medical supervision. The records that are made are filed away for use in the event of future compensation claims. It is unnecessary for me to point out that this is not practicing good medicine.

It goes without saying that the ideal hearing conservation program would entail the removal of the noise at its source. The extent to which these measures can be expected to decrease noise levels varies with the machines, the operations, and the physical plant and is a matter better left to the acoustical and industrial engineers. In the areas where noise levels cannot be effectively reduced by means presently available, the hearing of workers can be protected by the use of ear plugs. Considering that any protective device to be inserted into the ear canal is essentially a foreign body, it becomes obvious that the supervision of this aspect of the hearing conservation program should be in the hands of medical personnel and that all necessary hygienic measures should be taken. It has been my experience that the big problem is gaining the acceptance and cooperation of the workers and of convincing them it is not a sign of weakness but only good sense to protect their hearing with ear protectors.

Summary and Conclusions

Occupational deafness is defined as hearing loss occurring during the course of, or as the result of, one's employment. The hearing loss may occur suddenly, as the result of direct traumatic injury or of explosions, blasts, or gunfire, or it may occur gradually, as the result of prolonged exposure to hazardous noise levels. As otolaryngologists, our interest and function is to conserve and protect human hearing. Therefore, it behooves us to meet the challenges of occupational deafness by active interest and participation in the various aspects of the problem.

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ANESTHETIC MANAGEMENT OF PATIENTS WITH RESPIRATORY DISEASE

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• *Respiratory disease in a surgical patient can represent a serious complication to the giving of anesthesia. Preoperative management must include correction of the underlying pulmonary pathology, where possible. For preanesthetic medication, the barbiturates are preferable to analgesics. While the anesthetic agent itself cannot be related to any adverse effects on preexisting pulmonary infections nor, alone, have influence on postoperative respiratory complications, it must still be admitted no presently available agent or technique is ideal. The selected procedure must therefore be considered in the light of its particular advantages (e. g., bronchodilating qualities, rapid postoperative response) over predicted disadvantages (e. g., anoxia, respiratory depression). Competent postoperative supervision, preventing interference with adequate respiration, completes the program of providing safe anesthesia for patients with respiratory disease.*

One of the most frequently encountered problems in clinical anesthesia is that of the patient with respiratory disease. This problem deserves our careful attention. Unless it is successfully solved, the patient is subjected to an increased operative and postoperative morbidity and mortality, or surgery is so limited that the indicated procedure cannot be accomplished. Recent advances have been made that offer help in dealing with these patients. Although much yet remains to be learned, it is appropriate to consider some of the clinical ramifications of developments and, by combining them with older and well-recognized principles, to formulate a modern approach to this ancient problem. To limit an otherwise vast and complicated field, emphasis will be placed on those patients in whom the respiratory disease represents an incidental, albeit serious, complication to extrathoracic surgery.

Preoperative Management

Unless patients with respiratory disease are properly prepared prior to surgery, their anesthetic management during surgery will always be less than satisfactory. Preparation consists of correcting underlying pulmonary pathology insofar as possible and of eliminating factors that may increase the possibility of postoperative respiratory complications. Extrapulmonary causes of decreased ventilation must be sought out, for they are often reversible. Pleural or ascitic fluid should be removed by paracentesis, and obesity must be eliminated by an enforced program of weight reduction.

Respiratory infections must be controlled. In the upper respiratory tract, control includes treatment of chronic sinusitis and avoidance of elective surgery during acute infections, such as the common cold. In infections of the lower part of the respiratory tract, antibiotics should be administered parenterally and by inhalation of nebulized solutions if necessary. Adequate drainage of purulent secretions from bronchiectasis or lung abscesses must be assured by the use of pulmonary detergents, postural drainage, and bronchoscopic aspiration when such treatment is indicated. Patients with bronchiectasis should be operated on only after they have been able to spend several hours in the morning coughing and raising their own secretions. Actual or potential obstruction of the respiratory passages must be corrected. Patients with asthma should be desensitized to the offending allergen if possible and treated, if necessary, with cortisone and bronchodilating drugs.

Severe emphysema represents a serious and increasingly frequent complication. Because alveolar ventilation is inadequate to remove carbon dioxide, patients with emphysema have varying degrees of respiratory acidosis. Pulmonary infection may be superimposed. There may also be increased resistance to blood flow through the lungs, resulting in cor pulmonale with right-sided heart failure. Preoperatively, any myocardial decompensation is an indication for digitalization in these patients. Any infection is an indication for antibiotic therapy.

A potent carbonic anhydrase inhibitor, acetazolamide (Diamox), may be used preoperatively to decrease the respiratory acidosis. By interfering with normal renal electrolyte excretion, acetazolamide produces a bicarbonate diuresis. The resultant fall in plasma bicarbonate level is associated with a decrease in plasma pH and a lowering of abnormally high car-

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bon dioxide tensions. The exact mechanism by which acetazolamide improves alveolar ventilation remains incompletely defined, but the reduction in carbon dioxide tension may mount to 10 to 15 mm. Hg.[1] Although the beneficial effects of prophylactic administration of acetazolamide remain to be quantitated, its use in patients with severe emphysema who can be offered little else appears justified. It is especially appropriate in emphysematous patients about to undergo major upper abdominal surgery, for these are the patients whose respiratory exchange is most altered postoperatively. Acetazolamide, 250 to 750 mg. per day, may be given in one dose or two divided doses for four or five days preoperatively. It should be replaced by ammonium chloride on the day before surgery, so that the metabolic acidosis created by the acetazolamide may be lessened on the day of surgery.

Preanesthetic Medication.—Appropriate preanesthetic medication is of fundamental importance in the safe anesthetic management of patients with respiratory disease. Parasympatholytic drugs should be used in amounts somewhat in excess of the normal to reduce otherwise copious and troublesome secretions. Preanesthetic sedation should be obtained with drugs that not only produce a sense of mental relaxation and detachment but also do so without impairing ventilation. In carefully controlled studies, Lasagna and others[2] have shown that narcotics are far less satisfactory and predictable producers of euphoria than are barbiturates. For this reason alone barbiturates are preferable to analgesics for preanesthetic medication.

Also, Eckenhoff and others[3] have demonstrated that all commonly used analgesics depress respiration when given in therapeutic amounts to normal patients. Depression occurs to the extent that carbon dioxide tensions are invariably elevated, but it does not occur after hypnotic doses of barbiturates. In patients already suffering from an inability to excrete carbon dioxide normally, the use of analgesics for premedication is ill-advised unless the patient has pain. Preexisting respiratory inadequacy will not only be accentuated by analgesics but also the desired sedation will not be as predictably attained as with the use of barbiturates.

Management During Anesthesia

Choice of Anesthetic Agent and Technique.—Before consideration is given to the pharmacological and physiological properties of anesthetics as they affect patients with respiratory disease, three rather negative but nonetheless fundamental principles should be emphasized. The first principle is that none of the presently available anesthetic agents or techniques is ideal. They all have their advantages as well as their disadvantages. For patients with respiratory disease, the most satisfactory agent will be the one that provides advantages outweighing disadvantages, so that the over-all risk to the patient, although of necessity not eliminated, is diminished.

Secondly, anesthetic agents per se have no influence on the incidence of postoperative respiratory complications. For example, inguinal herniorrhaphies performed with the patient under spinal or local anesthesia are followed by respiratory complications with the same frequency as those performed with the patient under ether anesthesia.[4] Site of surgery, age, sex, body build, and, as Dripps and Deming[5] so aptly demonstrated, the care and ability with which the anesthesia is administered are all factors that do influence the development of postoperative respiratory complications. The anesthetic itself does not. Thirdly, although preexisting pulmonary infections (e. g., tuberculosis) are adversely affected by anesthesia and surgery, the degree to which they are influenced is not related to the particular general anesthetic agent used.[6] The pharmacological and physiological effects of anesthetics on the respiratory system can be discussed only with these three basic concepts in mind. They are prerequisite to an objective and scientific approach to the problem.

Use of Ether: Ether, the most potent inhalation anesthetic commonly used today, can be administered with a concentration of oxygen higher than can be used with any other agent. Surgical anesthesia with muscular relaxation is maintained with 4% ether and 96% oxygen in the inspired air. This high concentration of oxygen may prove advantageous in certain patients with severe pulmonary disease. Ether is also the only general anesthetic that, when given in concentrations adequate for moderate or light planes of surgical anesthesia, does not invariably cause depression of respiration to the point where respiratory acidosis supervenes.[7] Alveolar ventilation may actually be increased by ether, except in the deeper planes of anesthesia.

Respiratory acidosis can and most certainly does occur during the administration of ether, but it is neither as frequent nor as severe as that present with equal depths of anesthesia obtained with other agents. In patients with respiratory disease, this is a significant advantage. When and if respiratory acidosis does occur under light ether anesthesia, its presence may be, and usually is, clinically detected by alterations in the respiratory pattern. The sensitivity of the respiratory center to elevations in carbon dioxide level is depressed by higher concentrations of ether,[8] but during light anesthesia this depression is not severe enough to prevent completely the hyperventilation of respiratory acidosis. Simple and reliable objective methods of rapidly determining alveolar carbon dioxide tensions under clinical conditions are not available. The ability to recognize clinically and so to treat respiratory acidosis during moderate or light ether anesthesia is an invaluable aid in managing patients with respiratory disease.

The major disadvantage of ether as a general anesthetic in patients with respiratory disease is that recovery may be prolonged. Prolonged recovery occurs most frequently after long operations, in patients with emphysema, and after the administration of ether by the inexperienced. Recovery from ether anesthesia is not, however, accompanied by the same respiratory depression that follows recovery from equal depths of anesthesia produced by other general anesthetic agents. During the period of recovery from ether anesthesia there may be an increased production of mucus, but, as already indicated, this does not add to the is a matter for serious consideration in this day of increasingly complex anesthetic techniques. Since both methods are, however, satisfactory when correctly employed, the decision of which to use will usually depend upon the philosophy and training of the anesthetist and the financial resources of the hospital. From a practical point of view, at the present time it is more important to spend time, effort, and energy emphasizing the necessity of adequate ventilation and how it may be manually attained rather than to change anesthetists into mechanics versed in the mechanical problems and idiosyncrasies of various pumps, valves, and flywheels. It is economically certainly more feasible. The ultimate welfare of the patient will also be increased.

There is only one situation in which use of certain types of mechanical respirators has distinct advantages over manually performed ventilation. That situation occurs in patients with decreased cardiac output. During inspiration there normally exists a negative intrathoracic pressure that aids in venous filling of the right side of the heart. This pressure is eliminated by methods of artificial ventilation devoid of any negative phase and consisting solely of intermittent positive pressure. Patients whose cardiovascular status is precarious may react adversely to such positive pressures by showing further falls in cardiac output and blood pressure.[14] Since manual control of respiration eliminates negative pressures throughout the respiratory cycle, a mechanical ventilator providing negative pressure during expiration should be employed in such patients.

Postoperative Management

Immediate Postoperative Period.—The immediate postoperative period is as critical for a patient with respiratory disease as the operative period. The importance of competent supervision in a postanesthetic recovery room staffed by specially trained personnel cannot be overemphasized. Attention is centered on the prevention or correction of any interference with adequate respiration. Depression of the respiratory center caused by analgesics given during surgery is to be counteracted by use of specific antagonists such as nalorphine hydrochloride or levallorphan (*p*-3-hydroxy-N-allylmorhinan) tartrate. If caused by barbiturates or inhalation anesthetics, respiratory depression must be compensated for by artificial ventilation until such time as the respiratory center regains its normal threshold.

Any inefficiency of the muscles of respiration due to muscle relaxants must similarly be compensated for by artificial respiration. Muscle relaxant antagonists such as edrophonium (Tensilon) chloride are not to be wholly relied upon, for, although they may be temporarily effective, their effects may wear off before normal muscle activity returns. The fundamental danger of respiratory obstruction caused by soft tissues, secretions, or vomitus must be constantly guarded against. Obstruction is still one of the foremost preventable causes of death in the immediate postoperative period. Administration of oxygen should be employed unhesitatingly. Carbon dioxide inhalation is unnecessary in the immediate postoperative period. Excessive carbon dioxide levels are often already present, especially in the patient with respiratory disease. Addition of further carbon dioxide may make matters worse.

Management in the Ward.—After the immediate postoperative period has passed and the patient has returned to the ward, the respiratory cripple still has many dangers to overcome. Prophylactic administration of antibiotics is often indicated in these patients. Repeated, thorough physical examinations of the chest should be performed, including x-rays when necessary. Patchy areas of atelectasis should be treated by forced coughing and hyperventilation, by frequent changes of position and by early ambulation. Larger areas of atelectasis are an indication for immediate bronchoscopy. Because of their action as respiratory depressants, analgesics should be used sparingly and only for the relief of pain, not as sedatives. After certain types of surgery, nerve blocks may be effective in relieving pain, thus avoiding the use of analgesics. If such blocks are utilized, they must be performed at frequent intervals with relatively short-acting local anesthetics of known safety. At the present time no safe local anesthetics are available that will provide anesthesia for more than a matter of hours.

The performance of a tracheotomy at the conclusion of surgery may add greatly to the safe postoperative recovery of selected patients with pulmonary disease. When the patient is unable to raise his own secretions either because they are so profuse or because he is so weak, a prophylactic tracheotomy may prove lifesaving. This procedure will also decrease respiratory dead space by as much as one-third or even one-half of its normal 150 cc. Reducing dead space by 50 cc. in an emphysematous patient with a fixed tidal volume of 300 cc. will increase the amount of inspired air available for alveolar ventilation by about 30%. As important as the decision to do a tracheotomy, however, is the quality of care devoted to the tracheotomy after it has been performed. Suction through a tracheotomy must be done aseptically, gently, and rapidly. If suction is not correctly performed, hypoxia ensues, tissues are traumatized, and secretions increased.[15] Special equipment is necessary to deliver high concentrations of humidified oxygen to a tracheotomy. Insertion of a nasal catheter through the tracheotomy tube is to be condemned. Routine tracheotomy care is not to be delegated to the routinely trained. It requires special instruction and meticulous attention.

Summary

Safe anesthesia for patients with respiratory disease depends upon careful evaluation of each individual case. The management will vary according to the type and severity of the pulmonary pathology, the site and nature of the proposed surgery, the pharmacological effects of the anesthetic agent, and the skill of the person administering the anesthetic.

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IMMUNIZATION OF INFANTS WITH LIVING ATTENUATED POLIOMYELITIS VIRUS

LABORATORY INVESTIGATIONS OF ALIMENTARY INFECTION AND ANTIBODY RESPONSE IN INFANTS UNDER SIX MONTHS OF AGE WITH CONGENITALLY ACQUIRED ANTIBODIES

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• Two types of living attenuated poliomyelitis virus were administered by mouth to 24 bottle-fed infants by adding the virus preparations to the formula. Sixteen received the SM strain (representing type 1), two received the TN strain (type 2), and six received both strains at different times. Ingestion of SM was followed promptly by an asymptomatic alimentary infection, demonstrated by isolating the virus from the feces. Repeated doses were necessary to establish the carrier state in three of these infants Ingestion of TN by two infants was followed similarly by the isolation of type 2 virus from the feces. All infants developed active immunity after the inapparent alimentary infection It was found safe to administer the virus to infants less than a month old. Two infants who had not received the virus were placed in cribs between those of other infants carrying SM but did not contract the infection The presence of homotypic antibodies congenitally acquired from the mother did not prevent an active response in infants who received an adequate amount of virus.

In the course of studies conducted during the past six years, approximately 500 individuals have received by the oral route the SM (type 1) and TN (type 2) attenuated strains of poliomyelitis virus. The largest group of recipients comprised children from 3 to 12 years of age who had no demonstrable antibodies to the type of virus being administered. In one instance, the TN strain was given to a 3-month-old baby who showed the presence of type 2 antibodies probably acquired from her mother. (No blood sample was obtained from this mother for antibody determinations.) This infant became an intestinal carrier after the oral administration of the virus and developed a high titer of neutralizing antibodies 28 days after the feeding of virus.[1] Thus, here was an example that congenital passive immunity did not interfere with multiplication of the virus in the alimentary tract or with the subsequent development of active immunity Further studies undertaken along similar lines indicated that immune serum globulin (human) administered simultaneously with the attenuated viruses (types 1 and 2) did not prevent intestinal carriage of virus or have any deleterious effect on the antibody response [2] These findings led to the present trial with infants under 6 months of age, most of whom had circulating antibodies derived from their mothers against the type of virus being fed. Clinical data have been presented elsewhere.[3]

Material and Methods

Strains of Virus.—The history and properties of the TN (type 2) and SM (type 1) strains have been described fully in extensive reports published elsewhere [2] and will not be repeated here.

Administration of Virus.—SM virus-infected tissue culture fluid, either undiluted or as a 1:100 dilution in saline solution, was mixed in equal parts with glycerin. The TN virus, in the form of a 20% suspension of mouse brain and cord, was also mixed with glycerin

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From the Viral and Rickettsial Section, Research Division, Lederle Laboratories, American Cyanamid Company (Dr Koprowski and Mr. Norton), School of Medicine, University of Pennsylvania, and Children's Hospital (Drs Hummeler and Stokes), Hunterdon County Medical Center (Dr Hunt), Medical Department, Clinton Farms (Dr Flack), and Research Department, New York State Department of Mental Hygiene, Letchworth Village (Dr Jervis) is a matter for serious consideration in this day of increasingly complex anesthetic techniques. Since both methods are, however, satisfactory when correctly employed, the decision of which to use will usually depend upon the philosophy and training of the anesthetist and the financial resources of the hospital. From a practical point of view, at the present time it is more important to spend time, effort, and energy emphasizing the necessity of adequate ventilation and how it may be manually attained rather than to change anesthetists into mechanics versed in the mechanical problems and idiosyncrasies of various pumps, valves, and flywheels. It is economically certainly more feasible. The ultimate welfare of the patient will also be increased.

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had responded with a high titer of type 2 antibodies. Although a very low level of type 1 antibodies was observed in the maternal blood (table 1), no antibodies were detected in the infant's serum, either at birth or at the age of 119 days, when he received $10^{4.1}$ T. C. D.$_{50}$ of SM virus This feeding was followed promptly by alimentary infection with type 1 virus lasting from the 3rd to the 70th days and by a marked rise in type 1 antibodies, as determined on the 42nd and 71st days after virus administration. There was no change in the already high level of antibodies against type 2 virus, but there was a decline in the level of type 3 antibodies

The other nine infants (table 1) had not previously been fed virus, and the amount of SM virus they ingested varied from $10^{2.8}$ to $10^{5.1}$ T. C. D.$_{50}$. Alimentary infection followed each feeding, and the virus was excreted for periods ranging from 55 days (infant no. 3) to 108 days (infant no. 1). A significant rise in homotypic antibody levels was observed in all cases, early in certain infants (as in no 5) and later in others (as in no. 8).

A comparison of the figures in the last two columns with those in the sixth and seventh in table 1 indicates that there was a decrease in type 2 (except for infant no. 8) and in type 3 antibody titers during the 44 to 87 days after the feeding with the heterotypic SM virus. The difference in the case of type 3 antibody titers was greater and the decline more pronounced.

Table 2 summarizes results obtained with infants who were 175, 117, and 86 days old when given $10^{4.8}$, $10^{4.8}$, and $10^{5.5}$ T. C. D.$_{50}$, respectively, of SM virus. The mother of infant no. 14 had a low (1:6) titer of type 1 antibodies, and at the time her baby was fed type 1 virus its serum antibody titer was <1:2. The same infant had previously received type 2 (TN) virus (see table 7), but the type 2 antibody concentration in his blood was rather low (1:16). Nine days after ingestion of SM virus, the type 1 antibody titer had risen to 1:256, and it was slightly higher 31 days after virus feeding. The unusually early (9th day) homotypic antibody response may have been related to the persistence of an antigenic stimulus from the administration of the heterotypic TN virus 28 days before (see table 7). The feeding of SM virus to infant no. 16, in addition to producing a slight homotypic response on the 9th day and a pronounced response on the 31st day, also seemed to stimulate a heterotypic antibody response to type 2, as evidenced by the increase in titer from <1:2 before the administration of virus to 1:16 on the 31st day after virus was ingested. The same phenomenon was not observed with respect to antibodies against type 3 virus, which decreased, in the course of 31 days, in a pattern similar to that shown in table 1. During the 37 days after the administration of type 1 virus to infant no. 18, the homotypic antibody titer rose and the type 2 antibody level remained unchanged (1:256), while antibodies against type 3 virus declined from 1:64 to 1:4.

The duration of fecal virus excretion did not seem to be influenced by the actual level of homotypic antibodies at the time the virus was administered, which ranged from <1:2 (infants 14 and 15, tables

TABLE 3—*Concentration of Type 1 Virus in Stools of Human Subjects Fed the SM Strain of Poliomyelitis*

Stools Collected and Pooled, Days After Virus	T D$_{50}$ Titer* of Fecal Material Obtained from Subject No																			
	1		2		3		4		5		7		8		10		13		15	
	MK†	He‡	MK	He	MK	He	MK	He	MK	He	MK	He	MK	He	MK	He	MK	He	MK	He
1-4	1.5	1.7	5.5	>4.7	5.2	4.7	4.2	4.7	4.7	4.7	2.5	neg	3.5	2.7	1.7	1.7	3.7	3.7	3.5	3.7
5-8	—	2.7	—	4.5	—		—		—		5.7	3.7	2.7	1.7	3.7	3.7	+	4.7	4.2	3.7
9-12	3.7	2.7	5.2	>4.7	4.5	>4.7	4.7	4.7	4.7	4.7	+	4.7	+		4.5	4.5	tox		2.7	2.7
13-16	5.2	3.7	3.7	3.7	4.7	>4.7	5.2	3.7	4.7	>4.7	4.5	3.7	3.8	3.7	2.7	1.7	5.5	>4.7	4.2	2.7
17-20	4.5	>3.7	3.5	3.7	4.2	3.7	4.7	2.7	4.5	2.7	+		+		2.2	1.7	4.5	3.7	—	2.7
21-24	4.7	2.7	4.2	2.7	1.7	2.7	3.2	2.7	3.2	3.7	4.2	3.7	3.7	2.7	3.7	2.7	4.5	3.7	3.7	
25-28	4.2	2.7	2.7	2.7	1.7	3.7	2.5	1.7	2.5	2.7	+	3.7	3.7	3.7	1.2		4.5	3.7	1.7	
29-32	3.5	2.7	2.5	1.7	—		—		—		3.7	3.7	1.2	1.7	1.5		+	0.7	2.5	
33-36	4.0		3.7	1.7	2.2	0.7	<1.0	<0.7	2.5	1.7	2.7	2.7	neg	1.7	3.2		2.5	1.7	1.7	
37-40	—	3.7	—	1.7	tox	0.7	tox	0.7	3.5	1.7	+	1.7	<1.0	1.7	2.7		—		1.7	
41-44	4.2	3.7	3.5	1.7	3.7	2.7	2.5	tox	<1.0	0.7	1.5	1.7	<1.0	1.7	2.5		1.2		1.5	
45-48	4.5	>4.7	2.2	tox	1.5	0.7	2.5	tox	1.0	0.7	+	1.7	neg	1.7	1.2		tox		2.2	
49-52	—	4.7	tox	1.7	<1.0	0.7	2.2	tox	1.7	tox	1.7	1.7	1.2	1.7	1.5		2.5	1.7	1.7	
53-56	4.2	4.7	tox	1.7	1.0	tox	1.5	tox	tox	tox	1.2	1.7	neg	neg	2.7		1.5	1.7	2.5	
57-60	—		neg	tox	neg	neg	+		neg	0.7	neg		—	neg	3.5		—		2.2	
61-64	2.7	>4.7	neg	tox	neg	neg	<1.0	neg	tox	tox	neg		3.0	2.7	3.5		2.7	3.7	1.7	
65-68	—	3.7	neg	tox	neg	neg	neg	neg	tox	tox	1.5		—		[illegible]		3.7	2.7	2.7	
69-72	3.5	3.7	neg	neg		neg	neg	tox		neg			neg		2.5		—		1.7	
73-76		2.7		neg						0.7	2.3		<1.0		neg		1.5		neg	
77-80	2.5	2.7								1.7	neg		neg		neg		neg		neg	
81-84	2.7	2.7									neg		neg				1.5			
85-88	3.5	3.7									neg		neg				2.5			
89-92	neg	1.7															+			
93-96	neg	0.7															1.0			
97-100	<1.0	0.7															<1.0			
101-104	3.0	1.7															neg			
105-108	neg	1.7															neg			
109-112	neg	neg															neg			
113-116	—	neg																		
117-120	neg																			

* + = non titrated virus; — = no sample, tox = toxic, neg = negative

† MK = monkey kidney

‡ He = HeLa

Table 4.—*Administration of Type 1 (SM) Virus to Infants Less than One Month Old*

Infant No.	Antibodies Before Virus Administration: Mother, Type 1	Mother, Type 2	Infant (At Birth), Type 1	Infant (At Birth), Type 2	Infant (At Birth), Type 3	Virus Administration: Infants' Age, Days	Amount T.C.D.$_{50}$*	Alimentary Infection, Days	Antibodies After Virus Administration: Days After Virus	Type 1	Type 2	Type 3
22	1:712	1: 362	1:1,024	1:1,024	1:64	27	3.8	5-12	37 52 65	1:256 1:178 1:256	1:712 1:256 1: 91	1:16 1: 4
17	1: 64	1:1,024	1: 64	1:1,024	1:16	22	5.5	2-34 41-48	37 67	1: 91 1:362	1:256 1:178	1: 4 1: 4
21	1:256	1: 362	1: 712	1:1,024	1:64	20	3.8	2-29	37 52	1:178 1:362	1:256 1:256	1:16 1:23
23	1: 64	1: 64	1: 23	1: 256	1:64	15	4.8	2-23	31 52	1:256 1:712	1: 23 1: 16	1:11 1:11
24	1:256	1: 362	1: 256	1: 256	1:64	11	4.8	2-23	31 52	1:178 1:256	1: 44 1: 16	1: 4
25	1: 91	<1: 8	1: 64	<1: 2	1: 4	10	4.8	2-93	31 52	1: 64 1:256	1: 4 1: 4	<1: 2

* T.C.D.$_{50}$ = tissue culture doses$_{50}$, expressed as logs to the base of 10.

1 and 2) to as high as 1:362 (infant 8, table 1). The concentration of type 1 virus in fecal material was determined by the titration of stool specimens in tissue culture. The results are given in table 3 for the infants reported in table 1. In order to evaluate results properly, determinations of virus content were carried out independently in two laboratories in different cities. Tissue cultures of monkey renal epithelium were used in one, and HeLa cells in the other. Comparison of values yielded by the two methods of virus titration indicated close agreement. The highest concentration of virus in stools was found within the first 16 days after feeding, confirming observations made previously with older children.[5] After the initial 16 days, the concentrations of fecal virus seemed to decrease; however, the duration and intensity of alimentary infection varied from subject to subject, with the duration ranging from 55 days (infant no. 3) to 108 days (infant no. 1).

Administration of Type 1 Virus to Infants Less than One Month Old.—Because the results obtained in the trials described above were encouraging, the "age limit" of candidates for virus ingestion was lowered to less than one month. Six infants 10 to 27 days old were given the SM strain in oral doses ranging from $10^{3.8}$ to $10^{5.5}$ T. C. D.$_{50}$ (table 4). The levels of homotypic and heterotypic antibodies before virus administration were somewhat higher than those in older infants (tables 1 and 2). Also, curiously enough, the titers of antibodies against types 1 and 2 in the cord blood of infants no. 22 and 21 were slightly higher than in the blood of their respective mothers. However, these differences may again reflect experimental errors in the neutralization tests.

With the exception of infant no. 25, the duration of alimentary infection with SM virus in this group was shorter than in the older group (tables 1 and 2). Whether this observation may be related to the high level of maternal antibodies in infants no. 21, 22, and 24 is difficult to state. It should be noted that infant no. 8 (table 1) excreted SM virus for 74 days, although the homotypic antibody titer before feeding was 1:362, i. e., slightly higher than that of infant no. 24.

There also seemed to be some relationship between the immunologic activation of the antibody system by the ingested virus and the level of antibodies acquired from the mother. An unequivocal rise in type 1 antibody titers was noted after virus feeding in the blood samples of infants no. 17, 23, and 25, whose initial antibody levels were not very high. In the remaining three infants of this group, who had high titers of type 1 antibodies at birth, response was delayed in comparison with other infants. For instance, the titer of type 1 antibody of infant no. 22 fell from 1:1,024 at birth to 1:256 37 days after virus ingestion. On the 52nd and 65th days after feeding, almost the same levels of antibody persisted. At the same time, the heterotypic antibody titers against types 2 and 3 declined. The fall of type 1 antibodies observed in blood drawn from infant no. 21 on the 37th day after virus administration was offset by a rise on the 52nd day. Finally, there was no difference in type 1 antibody titers between specimens obtained before and after the administration of virus to infant no. 24, while heterotypic antibody titers against types 2 and 3 fell.

Since, in the past, an adequate immunologic response has always followed the establishment of alimentary infection with SM virus, there is no indication

Table 5.—*Repeated Administration of Type 1 (SM) Virus to Three Infants Who Failed to Develop Antibodies After First Administration of Virus*

Infant No.	Antibiotics Before Virus Administration: Mother, Type 1	Mother, Type 2	Infant, Age, Days	Infant, Type 1	Infant, Type 2	Infant, Type 3	Virus Administration: Feeding No.	Age, Days	Days After 1st Administration	Amt. T.C.D.$_{50}$*	Excretion Days	Antibodies After Virus Administration: Days After Virus	Type 1	Type 2	Type 3
9	1:178	1: 712	At birth	1:256	1:1,024	1:64	1 2 3	24 70 112	... 46 88	2.8 2.8 4.3	None None 1-32	44 42 57	1: 16 1: 16 1:256	1:256 1: 91 1: 44	1:4 ... 1:4
11	1:256	1: 64	At birth	1:712	1: 16	1:16	1 2	26 68	... 42	2.8 4.1	None 3-24	44 42	1: 44 1:256	1: 4	1:4 1:4
12	1: 44	1:4,096	90	<1: 8	1: 64	<1: 8	1 2	106 152	... 46	<2.3 4.1	None 3-35	44 42	<1: 2 1:362	1: 16	<1:2

* T.C.D.$_{50}$=tissue culture doses$_{50}$, expressed as logs to the base of 10.

at present that infants less than one month old form an exception. The evidence of response may be slightly delayed in the youngest age group, particularly in cases where the level of congenitally acquired antibodies is very high.

Repeated Administration of Type 1 Virus.—Administration of $10^{2.8}$ T. C. D.$_{50}$ of SM virus to two infants who were 24 and 26 days old was not followed either by evidence of alimentary infection or by a rise in homotypic antibodies (no. 9 and 11, table 5). In addition, another infant 106 days old (no. 12) failed to become a carrier, and there was no rise in the level of type 1 antibodies after the administration of one drop of SM virus in 4 ml. of formula. The concentration of virus in the mixture was lower than the equivalent of $10^{2.3}$ T. C. D.$_{50}$.

To determine whether immunization failure was directly related to the small amount of virus in the ingesta, these three infants were given another virus feeding (table 5). This time no. 11 and 12 received $10^{4.1}$ T. C. D.$_{50}$ of virus, whereas the dose for no. 9 was kept low ($10^{2.8}$ T. C. D.$_{50}$). Subjects no. 11 and 12 promptly became intestinal carriers, and a marked rise in circulating type 1 antibodies followed. Infant no. 9 again failed to become an alimentary carrier, and his level of type 1 antibodies remained unchanged for 42 days. Finally, after a third feeding consisting of $10^{4.3}$ T. C. D.$_{50}$ of virus, both alimentary infection and a rise in homotypic antibodies were achieved.

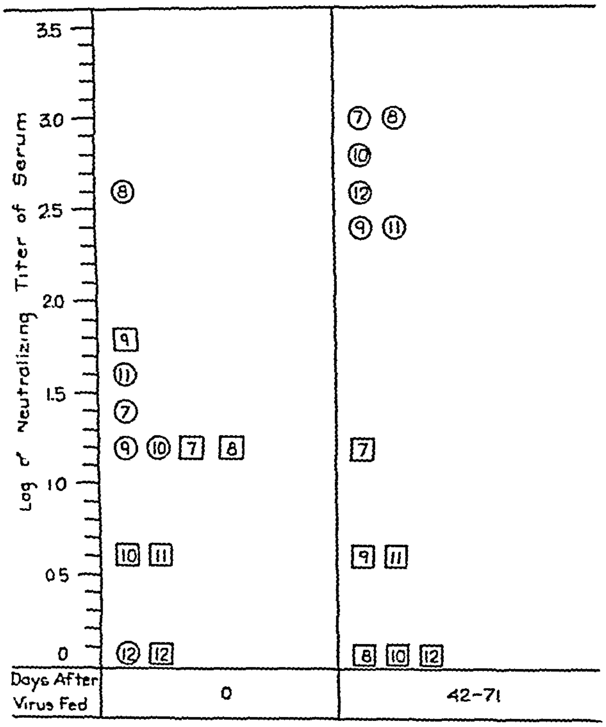

Fig. 1.—Increase of homologous antibodies after feeding type 1 with no simultaneous increase of type 3 antibodies. Numbers in circles, number of subject with antibodies against type 1; numbers in squares, number of subject with antibodies against type 3. Ages in months of infants at date of feeding were 1 (no. 8), 2 (no. 10 and 11), 2½ (no. 7), 3½ (no. 9), and 5 (no. 12).

Although these data are of meager statistical value, neither the age of the infants nor antibody status at the time of virus administration appeared to be responsible for the three "immunization failures." The roles of the relatively small amount of virus ingested and of some other possibly preexisting factor that may have prevented the virus from reaching a multiplication site in the intestinal tract may have to be considered (see Comment, below).

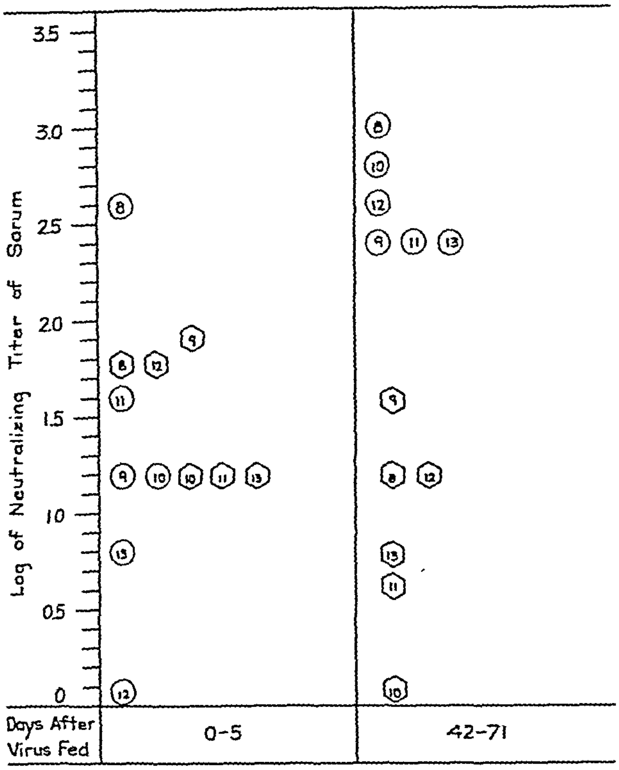

Fig. 2.—Increase of homologous antibodies after feeding type 1 with simultaneous decrease of type 2 antibodies. Numbers in circles, number of subject with antibodies to type 1; numbers in hexagons, number of subject with antibodies to type 2. Ages in months of infants at date of feeding were 1 (no. 8), 2 (no. 10, 11, and 13), 3½ (no. 9), and 5 (no. 12).

Fate of Homotypic and Heterotypic Antibodies.—The antibody titers in the serums of seven infants who received the type 1 virus are presented diagrammatically in figure 1 (infants no. 7-12) and figure 2 (infants no. 8-13). The clinical histories of these infants have been summarized in the preceding section of this report.

Figure 1 shows that after the administration of SM virus there was a marked rise in homotypic antibody titers. The rise was least significant in infant no. 8, whose serum showed a high level of congenital antibodies before the administration of virus. Within the observation period (42-71 days) antibodies against type 3 virus declined or remained the same.

Data on type 2 antibodies are presented in figure 2. In this case, the rise in homotypic antibody level was not accompanied by as marked a drop in type 2 as in type 3 antibody titers (see fig. 1). The serum antibody titer of infant no. 10 against type 2 virus fell to zero, while the decreases in the remaining serums were not of the same magnitude.

Lack of Contagiousness of SM Virus.—In clinical trials described elsewhere,[2] transmission of fecal SM virus occurred in very few cases and only after a rather initimate contact between "donors" and "recipients." The same question was investigated on a smaller scale under the conditions of the present study.

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	Antibodies Before Virus Administration					Virus Administration			Antibodies After Virus Administration			
	Mother		Infant (At Birth)									
Infant No.	Type 1	Type 2	Type 1	Type 2	Type 3	Infants' Age, Days	Amount T.C.D.$_{50}$*	Alimentary Infection, Days	Days After Virus	Type 1	Type 2	Type 3
22	1:712	1: 362	1:1,024	1:1,024	1:64	27	3.8	5-12	37	1:256	1:712	1:16
									52	1:178	1:256	1: 4
									65	1:256	1: 91	
17	1: 64	1:1,024	1: 64	1:1,024	1:16	22	5.5	2-34 41-48	37	1: 91	1:256	1: 4
									67	1:362	1:178	1: 4
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									52	1:362	1:256	1:23
23	1: 64	1: 64	1: 23	1: 256	1:64	15	4.8	2-23	31	1:256	1: 23	1:11
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									52	1:256	1: 4	

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TABLE 5.—*Repeated Administration of Type 1 (SM) Virus to Three Infants Who Failed to Develop Antibodies After First Administration of Virus*

	Antibodies Before Virus Administration						Virus Administration					Antibodies After Virus Administration			
	Mother		Infant												
fant No.	Type 1	Type 2	Age, Days	Type 1	Type 2	Type 3	Feeding No.	Age, Days	Days After 1st Administration	Amt. T.C.D.$_{50}$*	Excretion Days	Days After Virus	Type 1	Type 2	Type 3
9	1:178	1: 712	At birth	1:256	1:1,024	1:64	1	24	...	2.8	None	44	1: 16	1:256	1:4
							2	70	46	2.8	None	42	1: 16	1: 91	...
							3	112	88	4.3	1-32	57	1:256	1: 44	1:4
11	1:256	1: 64	At birth	1:712	1: 16	1:16	1	26	...	2.8	None	44	1: 44		1:4
							2	68	42	4.1	3-24	42	1:256	1: 4	1:4
12	1: 44	1:4,096	96	<1: 8	1: 64	<1: 8	1	106	...	<2.8	None	44	<1: 2		<1:2
							2	152	46	4.1	3-35	42	1:362	1: 16	—

* T.C.D.$_{50}$=tissue culture doses$_{50}$, expressed as logs to the base of 10.

no. 15, 19, and 20. Thus, one may assume that an immunologic response to TN virus occurred in infants no. 15 and 20 and probably in the other two infants. Determination of antibodies after a longer interval may dispel any doubts on this point.

Persistence of Immunity.—Serum samples were secured from five infants seven months and from one four months after the administration of type 1 virus (table 8). With two exceptions, no. 1 and 13, the same subjects also received TN (type 2) virus at the ages shown in table 8.

Data in the last three columns of table 8 indicate that feeding of type 1 virus was obviously responsible for the persistence of a high level of homotypic antibodies throughout the four-to-seven-month observation period. This is fully substantiated by the fact that during the same interval the type 3 antibody titers (last column, table 8) in every case except one dropped to <1:2. The point is even more clearly illustrated in figure 3, in which the rise in type 1 antibodies of five infants is contrasted with the simultaneous decrease or lack of increase in heterotypic type 3 antibodies.

After the administration of TN virus, there was a slight rise of type 2 antibody titer in infant no. 4 and a considerable rise in infant no. 3, whereas, during the five-month observation period, type 2 antibodies declined in the blood of infants no. 5. After an initial drop, there was a slight increase in the levels of type 2 antibodies in infants no. 1 and 13, who had received type 1 virus alone seven and four months previously. This may represent a remnant of heterotypic response to the type 1 feeding (see table 1), or it may indicate possible exposure to type 2 virus. However, no attempt was made to isolate fecal virus after the excretion of type 1 virus ceased, and no definite statement can be made. Clinical follow-up of these infants revealed normal development.

Comment

The results obtained in this study have shown that a single administration by the oral route of attenuated poliomyelitis virus to infants less than 6 months old will elicit alimentary infection and will activate an immunologic response, irrespective of the presence of passively transferred serum antibodies to the virus fed. Virus was fed to 24 infants; 16 received the SM (type 1) virus alone, 2 received the TN (type 2) virus, and 6 received both viruses administered weeks or months apart. Careful pediatric and nursing care of the infants failed to reveal objective signs of any ill-effects attributable to the ingestion of poliomyelitis virus. All of the infants who received the viruses at different ages showed gain in weight comparable to infants who were not fed virus.

Ingestion of type 1 virus was followed by prompt establishment of alimentary infection. That tissues of an infant 10 days old are able to support growth of poliomyelitis virus is not surprising per se, since cases of poliomyelitis infection with virulent virus have been described in infants shortly after birth after possible intrauterine infection.[6] A number of cases of poliomyelitis in infants less than a year old have also been reported in medical literature.[7]

Intestinal mucosa of children 6 to 15 years old previously has been found to be susceptible to direct infection with two plaque-forming particles of SM virus administered in a capsule.[2] This method of virus administration could not be applied in the present study, and virus feeding in liquid form was substituted. The results, though few in number, suggest that the inoculum had to exceed considerably two plaque-forming particles of virus in order to induce uniform alimentary infection in infants less than one month old. Although the number of infants fed virus at that age was too small to permit definite conclusions, SM virus in concentrations in excess of $10^{-3.0}$ T. C. D.$_{50}$ seemed to prove uniformly infectious and immunogenic.

The seemingly higher resistance of younger infants may depend upon two factors. One could be related to a specific difference in cell physiology during the first month of life. Thus, in a baby 30 days old or less, the virus-cell relationship may not be the same as that in older infants and children and may adversely affect the rate of multiplication of the virus, viz., infant no. 22 (table 4), who excreted the virus only between the 5th and 12th days after feeding. A direct relationship between age and susceptibility to poliomyelitis infection has been observed in laboratory animals,[8] and the relative infrequency of poliomyelitis infections among young infants has been noted.[7]

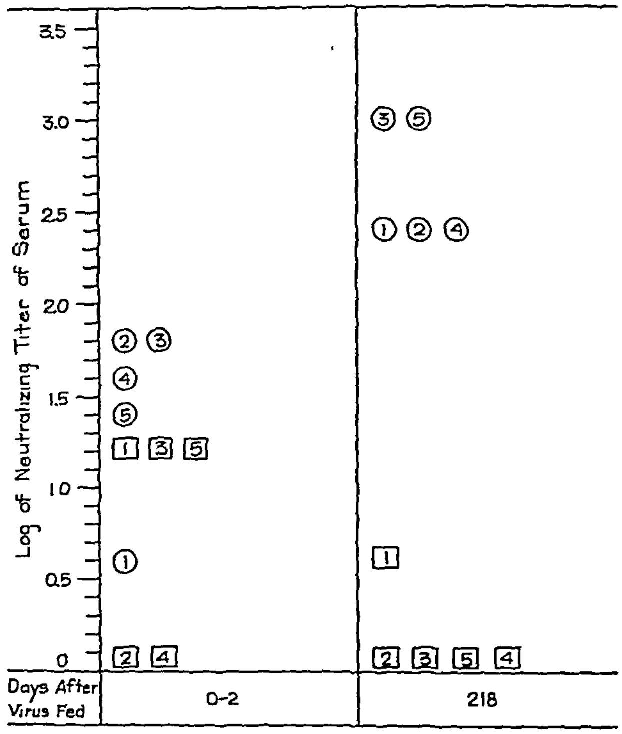

Fig. 3.—Increase of homologous antibodies after feeding type 1 with no simultaneous increase of type 3 antibodies. Numbers in circles, number of subject with antibodies to type 1; numbers in squares, number of subject with antibodies to type 3. Ages in months of infants at date of feeding were 1 (no. 1), 2 (no. 3 and 5), and 3 (no. 2 and 4).

The second factor to be considered is the amount of congenitally acquired homotypic antibodies. The concentration of these was higher in infants at the age of 30 days than in older infants and children or after administration of immune serum globulin.[2] However, in studies on passive-active immunization of primates, Bodian[9] observed that the presence of passive antibodies, even at high levels, did not interfere with the establishment and course of ailmentary infection with poliomyelitis virus but did prevent viremia and invasion of the central nervous system. In the present study, no. 22 was the only infant who had a titer of passive antibodies to type 1 as high as 1:1,000, which may be related to the short duration of SM virus excretion in his case.

Serum antibody titers of the two infants (no. 9 and 11, table 5) who failed to develop alimentary infections after the first administration of a small amount of virus or of those who showed a slightly delayed rise in antibodies after virus administration were also high in comparison with those of the remaining subjects (table 1) of the same series. From present data, it appears doubtful that in infants less than one month old a high titer of passive antibodies will consistently prevent alimentary infection with a small amount of type 1 virus. Because of the small number of subjects in this trial, it was not possible to determine what concentration of antibodies might influence the duration of alimentary infection. Whichever of the factors—relative lack of susceptible cells or high titer of serum antibodies—was in operation, feeding of adequate amounts (in excess of $10^{-3.0}$ T. C. D.$_{50}$) of SM virus resulted in inapparent infection and immune responses.

The administration of type 2 (TN) virus to eight infants led to a rise in homotypic antibody titers in the blood of five. The response of the remaining three, who received $10^{2.8}$ mouse P. D.$_{50}$ of the virus, will have to be evaluated from the results of neutralization tests to be performed on blood samples collected in the future. The two factors mentioned above (in connection with the administration of type 1 virus) conceivably may play a role in this case also, and perhaps feeding larger amounts of virus will yield more uniform results.

Changes in type 2 neutralizing antibody levels such as occurred in subjects who were infected with type 1 virus have been reported before by several investigators.[10] In the present study, among 16 infants who received the attenuated type 1 virus, type 2 antibody titers increased in five cases and the titer failed to decline in two additional cases. The heterotypic rise was maintained in the blood of two infants four and seven months after administration of type 1 virus (table 8). Similar changes did not occur in type 3 neutralizing antibodies, which were found to decline gradually and which reached levels below detection in the blood of infants at the age of 7 to 10 months. There was also no effect on the development of type 1 antibodies after administration of type 2 virus to three infants who had no preexisting type 1 antibodies. Thus, it may be concluded within the limits of these data that a response to SM virus feeding may be broader than a response solely to the type causing alimentary infection.

With the current trial included, attenuated strains of poliomyelitis virus have been given to infants, children, adolescents[11] and to adults (Sabin[12]). As far as can be judged, none of the subjects belonging to these different age groups showed any ill-effects that could be attributed to the ingestion of live virus.

For a more extensive clinical trial, the youngest age group is the most desirable, since it represents a relatively immobile population in which the possibility of transmission of the virus from one subject to another is more remote (*see* table 6). The presence of passive immunity will not prevent an active response if an adequate amount of virus is administered, and "blending" of the two types of immunity may circumvent the danger of exposure to virulent virus at an age when congenitally acquired antibodies tend to diminish or disappear. Follow-up studies over a much longer period of time[5] may indicate or give substance to the hope that the level of homotypic antibodies induced by the ingestion of virus in the first year of life may confer permanent protection.

Summary

Living attenuated poliomyelitis virus was administered by the oral route to 24 infants. Sixteen received SM (type 1) virus alone, two the TN (type 2), and six both viruses at different times. All the infants were under 6 months old; the ages of six were between 10 and 27 days. Most of them had antibodies acquired from their mothers to the virus fed. All infants developed active immunity after inapparent alimentary infection. High levels of homotypic antibodies caused by the feeding of virus were maintained during an observation period of seven months.

Box 149, N. Middletown Rd. (Dr. Koprowski).

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FETAL MORTALITY IN CESAREAN SECTION

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• *The gross fetal mortality associated with cesarean sections ranged from 4.5 to 15.6% in 13 institutions. The causes of death and indications for sections have been reviewed in detail for the last 16 years, covering 569 sections, at University of California Medical Center. The maternal mortality has been reduced by such factors as briefer trials of labor, blood transfusion, and new surgical techniques, but the fetal mortality has not shown corresponding improvement. Erythroblastosis, congenital anomalies, and atelectasis with its complications accounted for many deaths occurring within an hour after birth. Prematurity, however, is the largest single contributing factor to the high mortality rate. An accurate appraisal of arrival at term is important in order that a premature infant will not be delivered by ineptly timed and purely elective section.*

A striking and continued reduction has occurred in maternal morbidity and mortality after cesarean section, as a result of medical advances in the past two decades; however, fetal salvage has not improved encouragingly. With increasing safety for the mother, popularization of cesarean section logically followed. Nevertheless, when it became apparent that operative delivery from above did not necessarily insure the survival of a healthy infant, a more conservative attitude developed with regard to indications for and timing of cesarean section.

The obstetrician need not be reminded of his obligation to both mother and infant for safe delivery. The obvious risks of prematurity must be accepted, however, when an urgent maternal indication for cesarean section is present. Yet, in cases where hasty elective surgery is performed for borderline disproportion or when repeat section is done too early, the supposed term child is occasionally immature and frequently dies. As a consequence, the fate of the infant after cesarean section is of timely and vital importance. We have, therefore, reviewed the experience with cesarean section at the University of California Medical Center, San Francisco, for the past 48 years, with special consideration of the period 1940-1955, inclusive, in an attempt to answer the question, "Does cesarean section insure the delivery of a normal, living child who will survive?"

For purposes of review and comparison, the uncorrected fetal mortality in a number of large published series is summarized in table 1. The high figures are quite startling. The notable factors in this series are the high incidence of premature infants and the mortality associated with the obstetric pathology that necessitated the section, as opposed to the increased hazard of abdominal delivery. Correction for these two elements would make a comparison of fetal mortality after vaginal delivery more meaningful, but we must look to the statistics in elective sections to supply these answers. Wolff and Roter,[1] reporting on 162 elective sections where a previous cesarean was the indication, indicated a mortality of 3 (1.85%) and morbidity of 17 (10.4%).

Cesarean sections performed on clinic and private patients at the University of California Medical Center in San Francisco for the past 48 years have been reviewed (fig. 1). Our experience with respect to maternal morbidity and mortality essentially parallels that of other centers. This was reported in part previously by Arnot[2] and King.[3] The introduction of antibiotics, improved methods of anesthesia, and obstetric advances have almost eliminated maternal mortality (one maternal death since 1938—a pregnancy complicated by disseminated lupus erythematosus) and have materially reduced maternal morbidity. A striking contrast between maternal and fetal mortality, however, is shown in figure 2. As the number of deliveries and cesarean sections has increased, the absolute number of deaths in infants has steadily climbed. These data are expressed in terms of percentage of infant mortality, and figure 3 clearly indicates that (1) infant mortality in cesarean section has shown little improvement over the years and (2) the mortality is still an appreciable and serious one. It would appear, therefore, that the risk of cesarean section is still considerable if the welfare of the mother and the infant are regarded critically. A comparison of fetal loss in deliveries by cesarean section with total fetal experience over a 10-year period shows that the gross perinatal mortality of babies delivered by cesarean section was 8.3% (corrected, 2.5%); the gross infant mortality was 2.5% (corrected, 1.8%); and the gross neonatal mortality was 0.8% (corrected, 0.6%). In order to shed further light on this problem of fetal mortality, our experience at the University of California Medical Center in San Francisco is reviewed in detail from 1940 to 1955 inclusive.

Obstetric Factors

As in other centers, infants have been lost here after surgical delivery who, we now believe, might have survived. An analysis of the causative factors is revealing. The method of cesarean section, as well as the type of anesthesia, plays a part in fetal mortality and morbidity. Table 2 discloses the types of operation used during the past 16 years, together with the method of anesthesia used. A graphic representation of the type of cesarean section done at this institution during the 48-year period, 1907 through 1954, is of

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genographic appraisal of fetal age, although fraught with variables and not always satisfactory, often can be of help in the timing of elective section.[4] For example, if proximal tibial and distal femoral epiphyses are not well visualized, further delay of surgery might be prudent, even though the dates themselves suggest a more advanced pregnancy. Cephalopelvic disproportion often indicates the need for surgical delivery. A trial of labor, however, should be required in borderline cases, especially when there are possible compensatory factors. Planned cesarean section prior to the onset of good labor at term has often been unnecessary and has resulted in the delivery of an immature infant. This applies also, we have found, to repeat cesarean section. A retrospective consideration of the indications for cesarean section in the 47 fatal deliveries between 1940-1955 shows that in 44 cases section was indicated from the patient's record; in 31, the timing was seemingly correct; in 9, section might have been done earlier; and in 4, section might have been postponed as baby was not at term (previous section only index used). In all fairness to the obstetricians involved, it must be admitted that a clinical situation may appear quite different in later review, particularly when only the history is available for subsequent appraisal. Nevertheless, it is our considered opinion that, in the greater interest of the child, certain of the operations probably should have been accomplished earlier and others delayed.

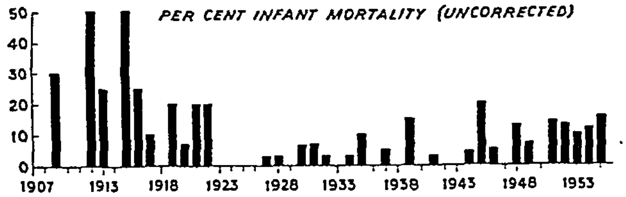

Fig. 3.—Infant mortality in cesarean sections, 1907-1955.

TABLE 3.—*Causes of Death in Twenty-seven Babies Who Lived One Hour or More (1940-1955, U. C. Medical Center)*

Atelectasis, including hyaline membrane and aspiration:		
Cause of death		14
Contributory	3	
Hyaline membrane	9	
Aspiration, massive	1	
Erythroblastosis		
Cause of death		5
Contributory	1	
Serious congenital anomalies		5
Diaphragmatic hernia	2	
Hydrocephalus	1	
Imperforate anus	1	
Anomalies of respiratory tree	1	
Nonviable (less than 800 gm.)		2
Intracranial hemorrhage		1

Fetal Factors

Over the last 16 years (1940-1955), 569 cesarean sections were performed with a total of 47 fetal deaths—a gross perinatal mortality of 8.2%. With correction for congenital anomalies incompatible with life, nonviable babies (less than 800 gm. [1.75 lb.]), erythroblastotic infants, and babies who died in utero before or during the operation, there were 15 deaths in 537 cases, or a corrected mortality of 2.9%. Of the 569 sections performed, 20 infants were either born dead or had never established respiration. Twenty-seven lived an hour or more, 16 were premature (weight under 2,500 gm. [5.5 lb.]), and 11 were full term; 20 were male and 7 female. The average length of life for the 27 babies was 2.5 days, the median being 1.7 days.

Table 3 relates the cause of death in the 27 babies who established respiration and lived an hour or more. Slightly more than half of this group died of respiratory causes, with hyaline membrane disease high on the list. This might be expected from the fact that more than one-half of these babies were premature. The six cases of erythroblastosis occurred during a one and one-half year period between 1946 and 1947, when cesarean sections were done before term (34-38 weeks) in instances where severe hemolytic disease of the newborn was suspected in the baby. This was before the use of the exchange transfusion became established. Thus, delivery by cesarean section of these babies served to superimpose prematurity onto the already existing hazard of erythroblastosis. With the use of cesarean section, our salvage of these babies was very poor and the procedure was abandoned. One of the six babies who died had hyaline membrane disease, and this, rather than erythroblastosis, was undoubtedly the cause of death. In the group of babies with congenital anomalies, it is interesting to note that both babies who died of diaphragmatic hernia were siblings, born a year apart. Of the two nonviable newborn infants, one weighed 780 gm. (1.75 lb.) and the other 450 gm. (1 lb.); the latter was, in fact, a deliberate therapeutic interruption of pregnancy. In spite of its small weight, the baby breathed and survived for 15 hours.

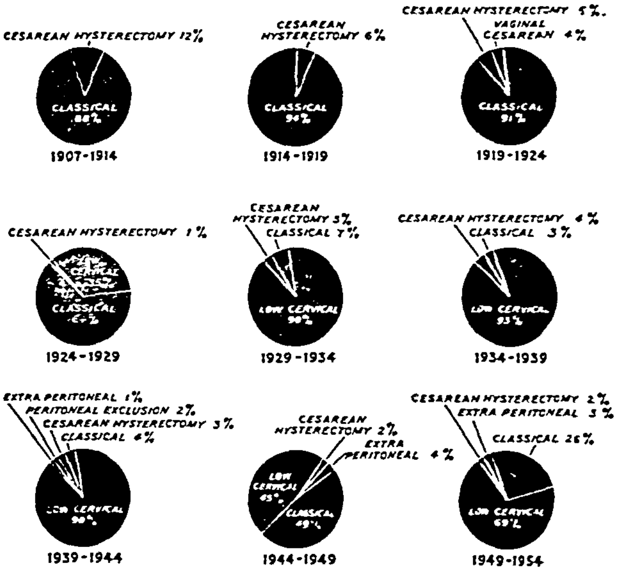

Fig. 4.—Type of cesarean section, 1907-1954.

Table 4 lists the 20 babies who did not establish satisfactory respiration. Almost all of these were born dead. There were 10 males and 10 females in this group; 9 were premature and 11 full term.

Of the 47 cesarean sections fatal to the infants, 14 were elective. The cause of death in these babies is shown in table 5. This group of babies should be considered critically in any series, because it generally excludes the serious obstetric catastrophes. Preventable deaths are apt to be found here as they were in our own series.

We have already mentioned the erythroblastotic babies in commenting on table 3. The three newborn infants who died of atelectasis, including hyaline membrane disease, were all infants who were considered to be at term, both by date and by palpation of the fetus. Cesarean section was done electively, the only indication being a previous section. At the time of delivery, all three of these babies were found to be small; two of them died of hyaline membrane disease and one of primary atelectasis. If the operative delivery had been postponed for several weeks in these cases, the outlook for survival of the babies would have been improved considerably.

TABLE 4.—*Indications for Section in Twenty Babies Who Never Established Respiration (1940-1955 University of California Medical Center)*

Baby No.	Wt. (Gm.)	Indications for Section
1	2,810	Partial premature separation of placenta
2	2,330	Obstructed labor; myoma; child dead before section
3	1,390	Severe preeclampsia
4	3,620	Prediabetic with eclampsia
5	4,800	Prediabetic with eclampsia
6	2,250	Partial premature separation of placenta
7	2,480	Premature desultory labor
8	2,680	Erythroblastosis, preeclampsia Previous section
9	1,300	Severe preeclampsia
10	1,900	Polyhydramnios, previous caesarean section (fear of rupture of uterus)
11	2,130	Compound breech
12	490	Diabetic; intercapillary glomerulosclerosis (Kimmelstiel-Wilson disease); pregnancy interrupted; sterilization
13	700	Partial premature separation of placenta
14	3,200	Massive intraperitoneal infection
15	2,800	Partial premature separation of placenta
16	2,900	Severe preeclampsia, premature separation of placenta
17	3,600	Ruptured uterus
18	2,500	Cervical fibroid; achondroplast
19	2,200	Sibling 18; achondroplast Section done early, mother suicidal
20	3,080	Severe complete premature separation of placenta; baby dead on admission to hospital

Table 6 lists the indications for cesarean section and the perinatal mortality for each indication over the last 16-year period for all cesarean sections performed. Corrections for infant mortality have been made by excluding babies who were known to be dead before the section was completed, babies who had congenital anomalies incompatible with life, and babies who were considered nonviable (less than 800 gm. [1¾ lb.]). The most common indication, by far, in this group was a previous section, and the mortality here was not a great deal higher than in the over-all obstretic experience for a comparable period.

The group with cephalopelvic disproportion was considerably smaller in our series than in most published studies from eastern teaching hospitals. This is hard to explain, although certain related factors might be a lower incidence of rickets in San Francisco and basic population differences.

As in other reported series, the group with the highest mortality was that in which premature separation of the normally implanted placenta necessitated an emergency cesarean section. The gross mortality figure of 62.5% for this group is more representative of what takes place than the corrected figure of 12.5%. The correction represents the eight babies who died of the separation before they could be delivered, the cause of death being the separation itself. In our experience, it would be more fair to state that, where serious separation of the placenta had occurred, the mortality was approximately 60%. Another group with high fetal loss was that in which cesarean section was performed because of toxemia and hypertensive disorders, but, in these cases, the maternal indication for delivery was most pressing.

TABLE 5.—*Causes of Death of Fourteen Infants Delivered by Elective Cesarean Section (1940-1955, University of California Medical Center)*

Erythroblastosis fetalis	5
Atelectasis, including hyaline membrane (these infants weighed 1,980, 2,200, and 2,800 gm.)	3
Polyhydramnios	1
Monstrosity	1
Nonviable fetus (450 gm.: late therapeutic abortion)	1
Diaphragmatic hernia	1
Baby dead in utero, previous cesarean section	2

Comment

Examination of infant perinatal and neonatal mortality rates in the United States over the past 50 years discloses the fact that today most infants are lost in the first three days of life. Bundesen[5] has stated that in the United States more infants now die in the first three days of life than during the remaining 362 days of the first year. He quotes the special committee on infant mortality of the Medical Society of the County of New York as stating that "The persistently high perinatal mortality rates stand foremost among the urgent problems on the agenda of Public Health workers." We would add to this: "and of obstetricians and pediatricians."

TABLE 6.—*Cesarean Section Indication and Total Infant Deaths (1940-1955, University of California Medical Center)*

Indication	Total No.	Gross		Corrected	
		Deaths	Rate, %	Deaths	Rate, %
Previous cesarean section	302	11	3.6	5	1.6
Contracted pelvis and/or disproportion	68	5	7.3	1	1.4
Placenta previa	34	3	8.8	2	5.9
Previous critical pelvic surgery	33	0	0	0	0
Toxemia and hypertensive disorders	29	10	34.4	4	13.8
Elderly primigravida	25	0	0	0	0
Prolonged and/or desultory labor	20	0	0	0	0
Premature placental separation	16	10	62.5	2	12.5
Breech presentation	5	1	20.0	0	0
Diabetes mellitus	6	1	16.6	0	0
Rh sensitization	4	3	75.0	0	0
Postmaturity	4	0	0	0	0
Other	45	3	6.6	1	2.2

In examining the causes for the high perinatal mortality and, specifically, the reasons for no decline in recent years, one must focus attention particularly on the special groups of babies who contribute to this loss. Foremost among these are the premature infants, but another important group is that which has been examined in the preceding tables, i.e., the babies born by cesarean section. Their gross perinatal mortality of 8.2% is more than three times that of the gross infant mortality of all groups. The two outstanding causes for this high mortality are (1) prematurity and (2) depression of the fetal respiratory center brought on by hypoxia or toxic states of the mother.

Prematurity is frequently unavoidable. The situation is often one of obstetric catastrophe, such as abruptio placentae with supervening massive hemorrhage, which necessitates immediate delivery—preferably by section. Thus, the baby arrives quite prematurely, sometimes before it is viable, or at the state of maturity where the chances for survival today are not much more than 50%. However, among this group of "unavoidable prematures," one must recognize a smaller category but, nevertheless, one about which something can be done—namely, those who, through an error in dates and misjudgment of fetal weight and maturity, are delivered prematurely by elective section (three in our series). The loss of these babies, in a situation where prematurity plays an important role in their death, is truly an avoidable tragedy. One of the sad obstetric realities is that we are, as yet, ignorant about the causes of the onset of labor. It is difficult, moreover, to know when a woman has arrived at term. We believe it is better to allow the woman to go into labor, in most instances, and to perform the operation as soon as true labor starts. The pediatrician can contribute expert postdelivery care to the premature infant, but this is not nearly as promising as the reduction of the loss of these babies by the avoidance of prematurity itself.

The second great cause of increased mortality in this group is hypoxia. This was certainly a critical factor in most of our stillborn babies Enumeration of mortality statistics and causes of death does not reveal the entire picture in this regard. We have not been able to include the morbidity of the group in this series, which would be of great interest in itself. Besides the babies who were lost, there were those who suffered irreversible damage, others had atelectasis and hyaline membrane disease and survived only after a stormy, prolonged course in the nursery.

Premature separation of the placenta and placenta previa are prominent causes of fetal mortality in this group. The considerable loss of babies of preeclamptic and eclamptic mothers suggests that the state of the mother may well have had something to do with depressing the baby. There is no question but that a good regional anesthesia, limitation of heavy analgesia, avoidance of oxygen lack before and during the cesarean section, together with proper timing so as not to allow a long period of intrauterine hypoxia before the section is performed, are all important factors in reducing the fetal loss in this group.

The pediatrician can help immeasurably by recognizing the true nature of the problem. Lavage of the stomach, gentle handling, expert resuscitation, a patent airway, and the delivery of oxygen into the infant's lungs by the least traumatic means possible will all increase the salvage of the jeopardized babies.

Summary and Conclusions

Examination of infant mortality associated with deliveries by cesarean section over the last 48-year period at the University of California Hospital revealed that 569 sections were performed, with a total of 47 fetal deaths and a gross perinatal mortality of 8 2%. Allowance for congenital anomalies incompatible with life, known nonviable babies, erythroblastotic infants, and infants who were known to have died in utero before or during the operation corrects the mortality to 2 9%.

Detailed review of causes of death for the 16-year period from 1940 through 1955 revealed that prematurity is the largest single contributory factor to the high mortality rate. Fetal hypoxia, due to interference with placental circulation, and the toxic state of the mother are other leading causes of death and morbidity. While appraisal of the woman's arrival at term is difficult, this decision is extremely important so that a premature baby will not be delivered by an ineptly timed, purely elective section. On the other hand, where an obstetric emergency produces a critical intrauterine oxygen deficiency, rapid delivery, often by cesarean section, is equally important in augmenting fetal salvage.

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Treatment of Obesity.—There was a considerable increase in weight loss in most of the patients receiving the Biphetamine capsule medication Over 70% of the patients taking Biphetamine lost three to four pounds and more in the three week interval, in contrast to about 85% of the patients previously on amphetamine tablets who lost less than three to four pounds during three weeks of therapy. In addition to the superior effect of the Biphetamine, this single dosage form of medication was more convenient than tablet therapy. It avoided the accidental failure to take a tablet or the unconscious avoidance of it. However, most patients will take a capsule in the morning, since their intentions are usually good at this time, and thereafter they are released from the responsibility of the need to take further medication. In addition, the therapeutic effect is smoother because of the elimination of the sharp rises and declines in blood levels, and it is thus more effective in alleviating hunger. . . . Suppression of appetite and loss of weight after administration of one capsule of this material are superior to the results obtained with an even greater dose of amphetamine in tablet form. Side-reactions with the amphetamine-resin complex are somewhat less than with tablet therapy. . . . . The amphetamine-resin complex fulfills a need for a product which releases the drug on a predictable basis for a period of 10 to 14 hours.—S. C. Freed, M D, J. W. Keating, B.S., and E. E. Hays, Ph D., Amphetamine-Resin Complex for Prolonged Appetite Suppression, *Annals of Internal Medicine*, June, 1956.

DIAGNOSIS AND TREATMENT OF EOSINOPHILIC GRANULOMA OF SKULL

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• *The diagnosis of eosinophilic granuloma of bone was made in five cases here reported; in each there was a circumscribed area of swelling or tenderness on a cranial bone, a characteristic circumscribed lytic lesion in the roentgenograms, and confirmation by microscopic examination of tissue obtained at operation. Headache attributable to extension of the tumor along meningeal blood vessels was severe in one case and present in two others; the intracranial pressure was normal and the neurological findings were negative in all cases. Surgical removal and subsequent irradiation to a total of 600 to 2,000 r in air was followed by healing and complete relief of symptoms. Eosinophilic granuloma should be considered as a diagnostic possibility whenever a patient presents a localized tenderness of the scalp or a lytic lesion of the skull.*

Eosinophilic granuloma of bone should be considered in the differential diagnosis of lytic lesions of the skull. First described as a clinical entity in 1940 by Otani and Ehrlich [1] and independently by Lichtenstein and Jaffe,[2] eosinophilic granuloma of bone has been the subject of increasing interest and controversy. Various authors feel that these solitary destructive lesions of the table of the skull are local evidence of a more generalized disease process. In 1942, Green and Farber [3] studied 10 cases and concluded that lipid histiocytosis of cholesterol type (Hand-Schüller-Christian disease), Letterer-Siwe's disease, and eosinophilic granuloma of bone were clinical expressions of the same basic disorder. Later, in 1944, Jaffe and Lichtenstein [4] advanced a similar thought but differed on etiology. In 1953, Lichtenstein [5] lumped these all under the single entity histiocytosis X. However, Otani and Ehrlich [1] felt that eosinophilic granuloma of bone, especially of the skull, should be classified separately from lipid histiocytosis of cholesterol type and Letterer-Siwe's disease, which carry a more serious prognosis and are of a more generalized nature. Eosinophilic granuloma of bone is primarily a disease of the reticuloendothelial system. At present, it is thought by some observers [6] to be infectious in nature, although no specific organism has been isolated.

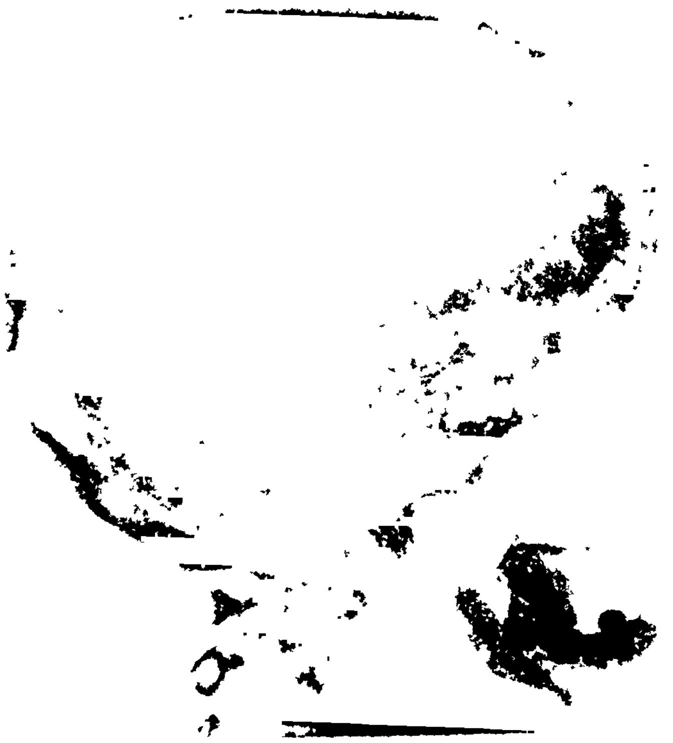

Fig. 1 (case 1).—Roentgenogram showing lytic lesion lying directly over branch of middle meningeal artery, which explains the symptoms of headache in this case.

Even as the controversy has arisen regarding the nature of this disease, so also have opinions differed on its treatment. Shuster and Flynn [6] favor surgical excision of the skull lesions, since drainage can be established if necessary. Gross and Savitsky [7] advise surgical excision in place of needle biopsy, since it provides a specimen for microscopic study and obviates roentgen therapy. Swain and Williams [8] describe perhaps the largest single skull lesion on record, which ended fatally but responded somewhat to surgery and roentgen therapy for a time. McCreary [9] records skin and bone involvement in a 2-year-old patient, with successful treatment with curettage of the bone and irradiation of the skin lesion. Curtis and Cawley [10] report multiple bone and skin lesions diagnosed by biopsy and clearing after irradiation. McCullough [11] claims good response to irradiation therapy of a skull lesion. He feels that this response supports the benign nature of this disease.

In the cases reported here, we wish to present the results achieved by combined surgical biopsy and roentgen therapy. The advantage of this plan of treatment is that it provides an adequate specimen for accurate microscopic diagnosis with the minimum of bone removal from the cranium. The roentgen therapy is followed by rather prompt regeneration of bone at the lesion site. The smaller the surgical lesion, the more rapidly this healing will occur. Since all of these cases consisted of solitary skull lesions that cleared remarkably after roentgen therapy, we, too, consider eosinophilic granuloma lesions of this character to be benign. However, we recognize that multiple lesions do occur. In these cases, the treatment is the same—surgical biopsy followed by irradiation. Sieracki [12] is also inclined to consider eosinophilic granuloma localized to bone as benign. It represents the successful confinement of the etiological agent.

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Diagnosis

The history of onset of eosinophilic granuloma of bone is usually insidious. The patient may notice a tender spot on the scalp. His attention may be directed to it by a recent trauma to the skull, which may prompt a routine skull film. This may immediately disclose the lytic lesion. Clinically, however, the area may be swollen, with localized tenderness. On the other hand, the swelling may be painless. At times, the lesion may appear so rapidly and break through the outer table of the skull so quickly as to simulate a primary malignant tumor such as a sarcoma. The solitary lesion of the skull is the most common manifestation of the localized type of eosinophilic granuloma of bone. When multiple foci are present, other bones are involved in the following order of frequency: ribs, skull, femur, vertebrae, pelvis, mandible, and humerus.

The disease is most common in children and adolescents but has been reported in infants, young adults, and even middle-aged patients. Headache is sometimes a prominent symptom. This is especially true if blood vessels of the scalp or the dura mater are involved. In one of our patients (case 1) headache was severe due to invasion of the temporal bone, dura mater, and a branch of the middle meningeal artery. When a biopsy specimen of this lesion was examined, it was found to surround the artery and to be invading the dura mater. After its removal, together with a small segment of the dural branch of the artery, the headache disappeared. Blood-vessel involvement appears to be one cause of headache or localized tenderness of the scalp in these patients.

Neurological examination in our patients was negative. In none of these did the solitary, localized lesion produce any signs of increased intracranial pressure. Roentgenograms of the skull show a sharply circumscribed bone defect with geographical outline. The margins are well defined without surrounding sclerosis. Both tables are usually equally involved. Positive diagnosis must be withheld, however, until the surgical biopsy specimen has been examined microscopically. Microscopic examination reveals a loose stroma of reticular tissue with bone spicules and numerous eosinophils, leukocytes, and small lymphocytes with occasional multinucleated giant cells. No malignant change is seen. The following five case reports are illustrative of the therapy with combined biopsy and irradiation.

Report of Cases

Case 1.—The patient was a 38-year-old woman with a three-month history of left temporal headache, not throbbing in character, relieved by acetysalicylic acid (aspirin). There was no definite hemicrania or familial history of migraine. Neurological examination was essentially negative except for the finding of a small localized prominence over the left temporal region measuring about 1.5 cm. in diameter. There was no evidence of inflammatory change in the temporal artery on the affected side or the opposite side. Laboratory studies of the blood, urine, and serum were normal. Roentgenograms of the skull showed a lytic lesion over the left temporal bone about the size of a dime (fig 1). Chest films were normal. On Jan. 6, 1956, a biopsy specimen was taken from the left temporal bone lesion. This revealed eosinophilic granuloma that infiltrated the underlying dura mater and involved a branch of the middle meningeal artery. This area was clipped and the overlying granuloma removed and the bone curetted. Microscopic examination revealed eosinophilic granuloma that had involved the adventitial layer of the middle meningeal artery (fig. 2). There was also infiltration of the tumor into the area of the temporalis muscle. There were many large mononuclear cells and eosinophils in the adventitial areas of the small arteries. Sections of the tissue proper revealed many eosinophils, large mononuclear cells, and giant cells that appeared to be multinucleated. The patient received roentgen therapy immediately and was given 200 kv. of irradiation weekly to a total of 600 r in air. Her headache was completely relieved after the biopsy and clipping of the middle meningeal artery branch. There was gradual regeneration of bone after roentgen therapy. The patient has been seen in our outpatient department and had not had any recurrence after six months.

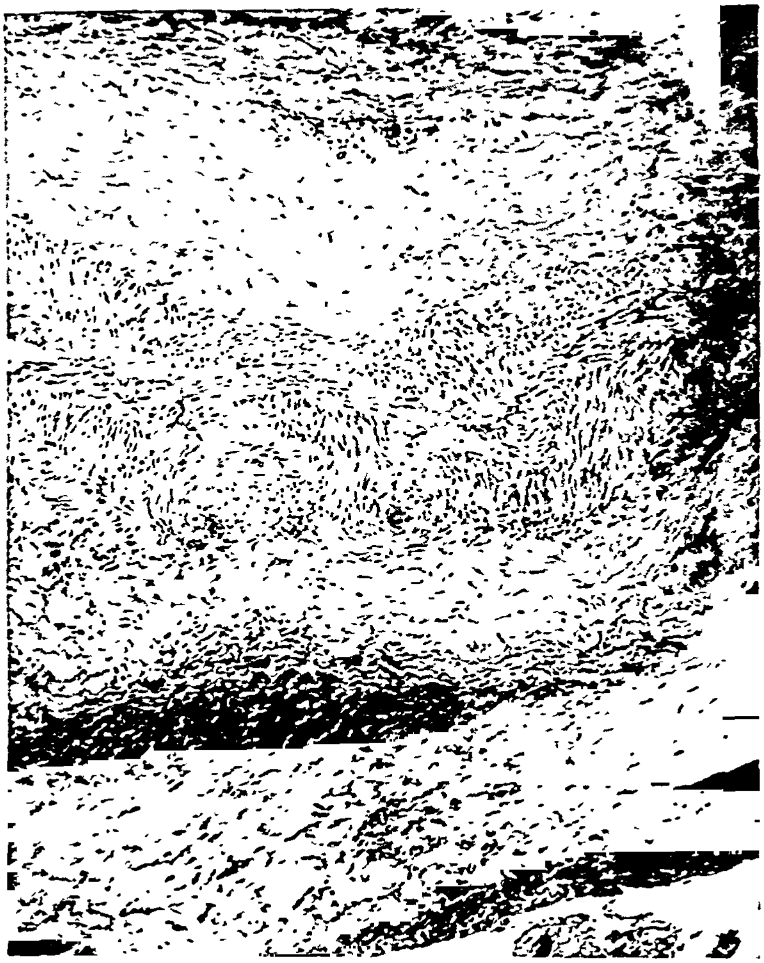

Fig. 2 (case 1).—Photomicrograph showing branch of middle meningeal artery. The eosinophilic granuloma surrounds the vessel but does not appear to invade the vessel wall (x 90).

Case 2.—The patient was a 6-year-old boy, first seen on Jan. 20, 1952, because of a swelling of the left eye of four months' duration. He had no visual disturbance and no pain. Neurological examination revealed an apparently normal 6-year-old boy, with no visual-field, funduscopic, or neurological abnormalities. Laboratory studies of the peripheral blood, urine, serum, and bone marrow were normal. Roentgenograms of the skull revealed an oval 1.5 by 1 cm. zone of destruction in the upper outer corner of the left superior orbital ridge. Chest films were normal. On Feb. 6, 1952, biopsy of the skull lesion revealed eosinophilic granuloma. A large amount of soft grayish tissue and periosteum was found. This was curetted for diagnosis. Microscopic examination showed the tissue to contain a conglomerate mixture of fibroblasts, epithelial cells, multinucleated giant cells, a few foamy histocytes, and a large number of eosinophils. The eosinophils were most prominent in the periphery of the lesion. The patient was given roentgen therapy of 100 r for six doses—a total of 600 r in air. After this there was a regression of the lesion and a gradual healing of the bone. Progress roentgenograms of the skull were essentially normal on Aug. 9, 1952, six months after treatment, and no recurrence was noted after four years of follow-up.

CASE 3.—The patient was a 32-year-old right-handed man who gave a history of headache for three months after he received a bump on the head while at work. There was no loss of consciousness, no bleeding, and no swelling, but the area struck, in the left parietal bone, continued to give pain. There was an associated frontal headache, dull and throbbing in character. Neurological examination was essentially negative except for slight tenderness over the left parietal area of the skull. Laboratory studies of the blood, urine, and serum were normal. A lumbar puncture was normal, with opening pressure 150 mm. H_2O. The cerebrospinal fluid was clear and colorless. The spinal fluid level of protein was 36 mg. and of sugar 72 mg. per 100 cc. The results of the Wassermann test were negative. An electroencephalogram and chest films were normal. Roentgenograms of the skull showed a 2-cm. rounded defect in the left temporoparietal area (fig. 3A.) On March 21, 1953, a surgical biopsy of the skull lesion was performed. This revealed eosinophilic granuloma. Microscopic examination showed a striking number of eosinophils intermixed with leukocytes and macrophages, scattered through a loose stroma of reticulated background (fig. 4 and 5). Bone spicules were present and showed marked scalloping, probably an index of the increased osteoclastic activity with very prominent cement lines seen in other bone spicules. No malignant change was noted. The patient was given roentgen therapy consisting of 100 r for nine doses and 200 r as a final dose, with a total of 1,000 r in air. Repeat roentgenograms of the skull taken July 11, 1953, showed evidence of healing in the left parietal bone (fig. 3B). Subsequent films, taken July 26, 1955, more than two years later, showed no evidence of the skull lesion and no recurrence elsewhere.

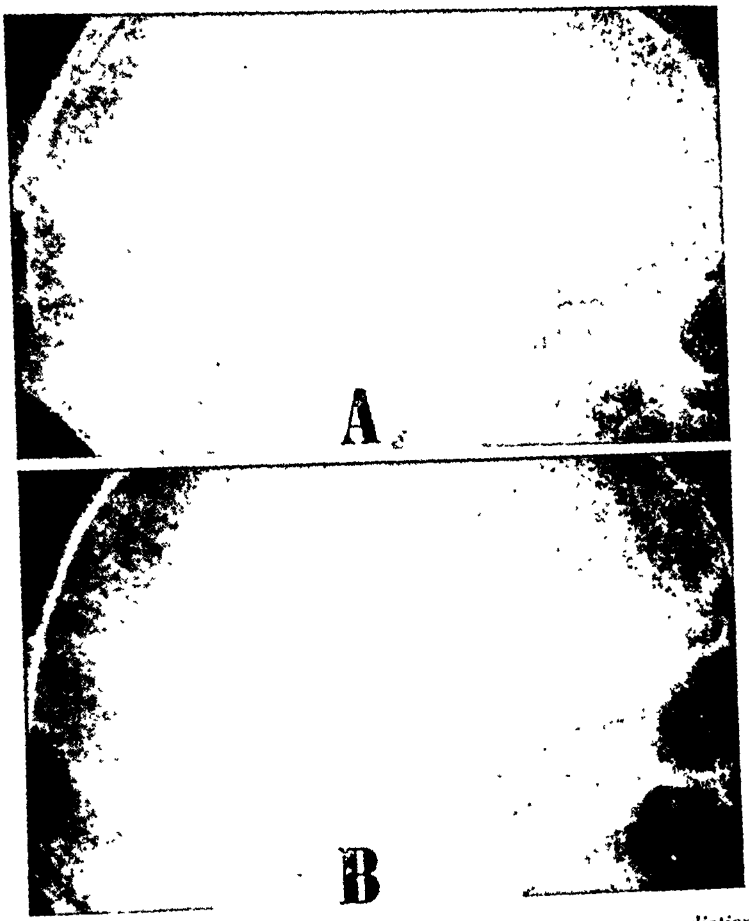

Fig. 3 (case 3).—*A*, roentgenogram of skull before biopsy or radiation therapy. *B*, roentgenogram of skull taken after radiation therapy with 1,000 r in air. Note complete healing of lesion in left parietal area. Film was en two years after therapy and shows no signs of recurrence.

CASE 4.—The patient was a 14-year-old right-handed boy who was in a fight on April 10, 1955. He suffered a blow to the left side of the head and was quite dizzy afterward. After this, he noticed a tender area in the left parietal region of his skull. Physical and neurological examination was negative. Laboratory studies of his blood, urine, serum, and blood chemistry were normal. A roentgenogram of the skull showed a radiolucent area in the left parietal region 2.5 cm. in diameter (fig. 6*A*). A chest film was normal. On May 18, 1955, biopsy and curettage of the lesion were performed. At operation the frozen section and imprint smear revealed eosinophilic granuloma, later confirmed on section. The lesion, measuring 2.5 cm. in diameter, was curetted up to the bony edge. Microscopic examination showed sections consisting of eosinophilic granuloma of the skull. These are composed of masses of cells set in a somewhat fibrous stroma. There were numerous eosinophils and a large number of nuclear cells. Occasional multinucleated giant cells were encountered. The remaining cellular structures were small lymphocytes, occurring in fairly large clumps. After biopsy and confirmation of the diagnosis by pathological section, the patient was given a series of two courses of radiation therapy, each consisting of 200 r at 10 different sittings. A total of 1,000 r in air was given over the left parietal area, and another course of 1,000 r in air was given in 200-r doses over the occipital area to a small second lesion. The patient has been free of any symptoms since irradiation, with no further head or skull pain. He has regrowth of bone in the former skull defect, as shown on the latest roentgenograms of the skull, taken one year later (fig. 6*B*). At follow-up, one year after treatment, no recurrence was noted.

CASE 5.—The patient was a 32-year-old right-handed female with a history of right supraorbital headache of one month's duration. She had occasional dizziness and a tender area over the right temporal area of the skull. Neurological examination was essentially negative except for the 2.5-cm. tender swelling in the right temporal area. Laboratory studies of the peripheral blood, urine, and serum were normal. Roentgenograms of the skull showed an irregular 1 by 1 cm. radiolucent area in the right frontal bone. A chest film was normal. On Oct. 23, 1954, a surgical biopsy was made of the skull lesion. A vascular and reddish purple lesion was curetted from the bone. The tumor extended through the inner and outer tables of the skull, but the dura mater was not involved. Microscopic examination revealed eosinophilic granuloma. The tumor was composed of eosinophils, with occasional neutrophils and plasma cells in a

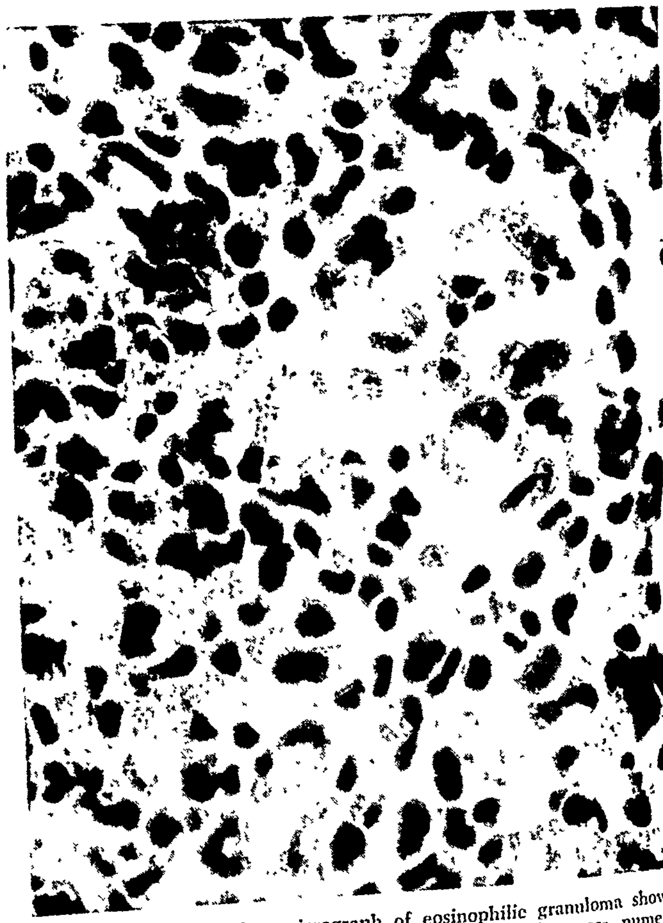

Fig. 4 (case 3).—Photomicrograph of eosinophilic granuloma showing loosely textured connective tissue stroma in which there are numerous eosinophils, giant cells, and histiocytes (x 710).

loose reticular stroma. The patient was given a total of 800 r in air. Her headaches and pain in the temporal region completely subsided, and she had no evidence of recurrence after 18 months. Repeat roentgenograms of the skull on July 26, 1955, showed no evidence of the previous lesion in the right frontal bone.

Comment

The diagnosis of eosinophilic granuloma of the skull often rests with the family physician or specialist who first sees the patient and suspects a lytic lesion. In any case of persistent localized tenderness of the scalp or localized headache, roentgenograms of the skull should be taken. This will almost invariably localize the lytic lesion and determine its size. The final diagnosis, of course, is a microscopic one after biopsy. In view of the unknown etiology of this lesion, no ironclad formula for its handling can be laid down. However, because it behaves in a benign fashion, as compared with Letterer-Siwe's disease and lipid histiocytosis of cholesterol type, it is deemed safe to handle it as a benign lesion. The cases presented tend to support this view. They were treated by surgical biopsy and irradiation, with immediate regression of the skull lesions. In the follow-up period, ranging from one to four years, no recurrence has been noted. However, should recurrence occur in later study, more radical therapy might be necessary. Until such time, it seems best to treat these lesions as outlined, i. e., by surgical biopsy and irradiation.

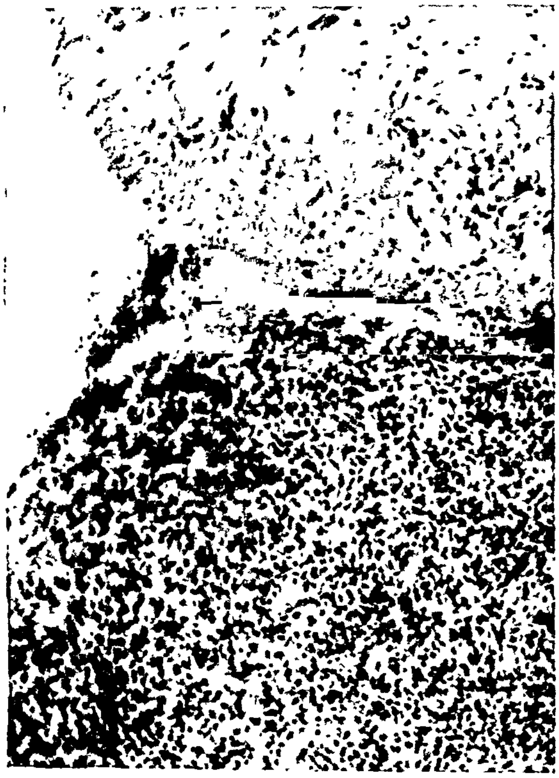

Fig. 5 (case 3).—Photomicrograph of eosinophilic granuloma showing junction of fibrous tissue and tumor (× 150).

Summary

Since 1952, we have seen five cases of eosinophilic granuloma of the skull. It is important to consider the possibility that this disease exists when there is any localized tenderness of the scalp or any lytic lesion of the skull. Since eosinophilic granuloma of the skull is frequently solitary and benign and carries a good prognosis, accurate diagnosis should be made by surgical biopsy, with removal of a specimen large enough for microscopic examination. The treatment is uniformly successful with roentgen therapy. Usually, a course of six exposures of 200 r in air is sufficient. The patient's scalp pain is relieved immediately after biopsy and irradiation. The regrowth of the bone of the cranium is usually demonstrated roentgenographically within six months.

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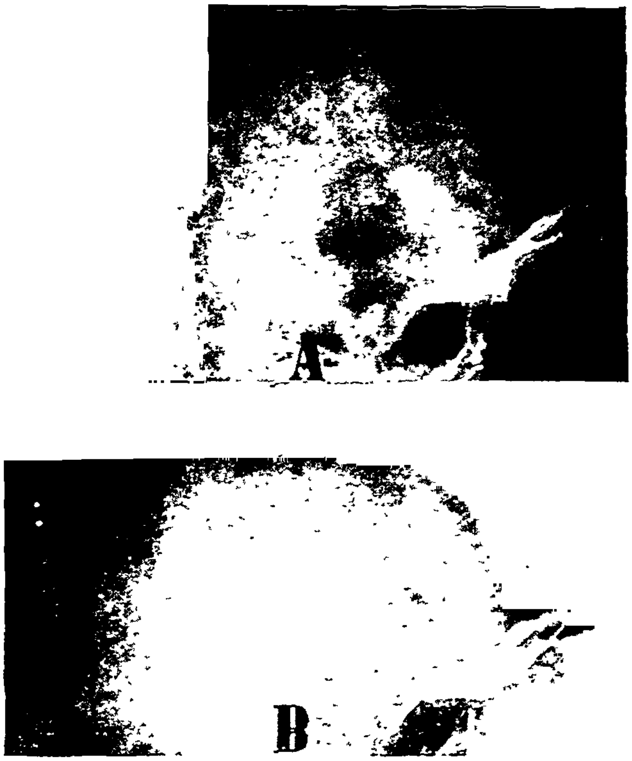

Fig. 6 (case 4).—*A*, roentgenogram of skull taken before therapy showing large lytic lesion in left temporoparietal area measuring 2.5 cm. in diameter. *B*, roentgenogram of skull taken one year after surgical biopsy and irradiation therapy with 1,000 r in air to lesion and a second course of 1,000 r in air to the occipital area for second lesion. Note almost complete healing of the lytic lesion and no evidence of recurrence.

Dr. Joseph E. Sieracki of the Department of Pathology, Henry Ford Hospital, procured and described the microscopic sections.

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ried out on 13 healthy household associates of the 7 patients. Specimens were also collected from three nonhospitalized patients in the community.

Throat and rectal swabs were placed in tubes containing 2 ml. of tissue culture nutrient medium. Specimens were frozen either immediately at -20 C or after 24 hours' storage in a refrigerator. Stool specimens were prepared as 10 to 20% suspensions in tissue culture medium. The turbid stool suspensions and the throat and rectal swab eluates were clarified by centrifugation. Spinal fluids were used without treatment. For virus isolation, a 0.2-ml. aliquot from each specimen was inoculated into trypsin-dispersed monkey kidney monolayer tissue cultures (Melnick[1b]) in 16-by-125-mm. test tubes. The cells were propagated in a growth medium consisting of 97.5% Hanks' balanced salt solution, 0.5% lactalbumin hydrolysate, and 2% calf serum, with 200 units of penicillin and 200 mcg. of streptomycin added per milliliter. At the time of inoculation, the growth medium was replaced with 0.9 ml. of maintenance medium consisting of Earle's saline solution, lactalbumin hydrolysate, and calf serum. Specimens were inoculated into each of three tissue cultures and the tubes incubated at 36 C.

TABLE 2.—*Recovery of Fourteen Cytopathogenic Agents in a Study of Aseptic Meningitis in Holland, N. Y.*

	Hospitalized Patients		Specimen*			Healthy Household Associates	
Family	Lab. No.	Age, Yr.	Stool	Throat	Cerebrospinal Fluid	No.	Agents Isolated
1	11	6	+	+	—	3	2
	15	17	+	—	—		
	16	11	+	—	—		
2	14	8	+	+	—	2	0
	17	8	+	—	—		
3	18	12	+	+	—	6	0
4	28	4	+	+	—	2	0

Totals	Stool	Rectal Swab	Throat	Cerebrospinal Fluid
7 hospitalized patients	7/7	N.D.*	4/7	0/7
13 healthy household associates	2/5	0/5	0/6	N.D.
3 nonhospitalized patients	1/3	N.D.	N.D.	N.D.

* + = positive; — = negative; N.D. = not done.

Microscopic observations for the appearance of viral cytopathogenic effect were made daily or every other day. Careful examination was made for evidence of cellular damage due to toxicity of the specimens. This was usually manifest within 24 hours. Stool inoculums were generally slightly toxic, while throat and rectal swabs were essentially nontoxic. Spinal fluids were also nontoxic and in fact appeared to have some nutritional value for the monkey kidney cells. Throat swabs and spinal fluids were considered negative at the end of a seven-to-nine-day incubation period unless there were changes in the kidney cells suggestive of viral effect, in which case the fluids were harvested and passaged a second time in tissue culture. Stool specimens or rectal swabs were considered negative only after two passages had been completed.

Identification of Agents Isolated.—The results of the virus isolation studies are tabulated in table 2. A total of 14 cytopathogenic agents were isolated. Virus was recovered from the stools of all seven hospitalized patients and from the throat swabs of four. No cytopathogenic agents were isolated from their spinal fluids. Two agents were recovered from stools of healthy household associates, while their other specimens were negative. One stool agent was recovered from a nonhospitalized patient. All 14 agents were examined in a tissue-culture neutralization test against prototypic poliomyelitis monkey antiserums. None of the 14 agents was neutralized by a mixture of the three types of poliomyelitis antiserums. It was therefore concluded that these agents were not poliovirus or a mixture of polioviruses.

Four stool agents (no. 11, 14, 18, and 28), from patients representing the four families studied, were examined in a virus neutralization test with Coxsackie prototypic antiserums of those types presently known to be cytopathogenic in tissue culture (types A9 and B1-5). None of these agents was neutralized by the above serums. In addition, the above four agents were inoculated into infant mice less than 24 hours old via the intraperitoneal route. There was no evidence of illness in the inoculated mice. In three instances, a second blind passage was made in infant mice with mouse brain-muscle suspensions; there was no apparent infection. Inoculation of the first-passage brain-muscle suspensions into tissue culture failed to demonstrate the presence of live virus and indicated a failure of the virus to survive through one passage in infant mice.

Since the Holland agents were not identifiable as poliomyelitis or Coxsackie viruses, according to both serologic and animal inoculation studies, they were designated at this point as orphan viruses. The following serologic studies were undertaken to elucidate the antigenic relationships of the 14 agents among themselves and to known ECHO virus types. Two of the fecal agents (no. 14 and 18) were selected for the preparation of specific antiserums. Rabbits were given 1 ml. of undiluted virus intravenously followed by five weekly doses of 1 ml. intramuscularly. Seven to 10 days after the last dose, the rabbits were exsanguinated by cardiac puncture. The antiserums thus prepared were capable of neutralizing 100 TCD_{50} of homologous virus in titers of 64 to 512. (All neutralization titers are expressed as reciprocals of the 50% serum dilution end-points.) All of the 14 orphan viruses were readily neutralized by either of the two Holland prototypic rabbit antiserums. It was thus apparent that the 14 orphan agents isolated in the Holland study were of the same serologic type.

In addition, the two Holland orphan strains were examined serologically with rabbit antiserums prepared against four other orphan viruses isolated from patients residing in other communities in western

New York who had had aseptic meningitis in 1955. Table 3 summarizes the results. It was found that the Holland agents were serologically related to two of the other four agents, one from Buffalo (no. 25) and the other from Springville, N. Y. (no. 8). The remaining two orphans from Batavia (no. 801) and Buffalo (no. 32) were found to be serologically alike but unrelated to the Holland group. For simplification, the Holland agents and serologically related orphan viruses were designated tentatively as Buffalo orphan prototype-1 (BOP-1), and the second serotype, representing the two orphan agents from patients no. 801 and 32, was designated as BOP-2.

Table 3.—*Serotyping of Orphan Viruses Isolated from Patients with Aseptic Meningitis*

Virus Neutralized (No.)	Antiserum: Holland, N. Y. 18	14	Other Isolations in Western N. Y. 25	8	32	801	Gamma Globulin
18*	+§	+	+	+	−	−	+
14*	+	+	+	+	−	−	+
25*	+	+	+	+	−	−	+
8*	+	+	+	+	−	−	+
32†	−	−	−	−	+	+	+
801†	−	−	−	−	+	+	+
ECHO Type 6	+	+	N.D.‡	N.D.	−	−	+

* BOP-1.
† BOP-2.
‡ N.D. = not done
§ + = positive, − = negative.

To determine relationship to presently known ECHO virus types, the 13 ECHO virus prototypes were examined in a virus neutralization test against BOP-1 and BOP-2 rabbit antiserums, with 100 TCD_{50} of each virus employed. ECHO virus type 6 was specifically neutralized by BOP-1 antiserum but not by BOP-2 antiserum. It was concluded that the 14 orphan viruses isolated from Holland patients with aseptic meningitis and their healthy family contacts, as well as two other orphan agents isolated from patients with aseptic meningitis, were serologically identical with the ECHO type 6 prototype. As has been noted in table 2, no viral agents were recovered from cerebrospinal fluid specimens from the seven Holland patients. However, during the investigation of the concurrent generalized outbreak of seasonal aseptic meningitis in western New York (July through September, 1955), a total of 10 orphan agents were recovered from cerebrospinal fluid specimens from hospitalized patients. Seven of these 10 agents have been found to be serologically identical with ECHO type 6.

Antibody Response in Patients

Poliovirus Antibody Studies.—The serums obtained during the acute and convalescent stages of the disease from the seven patients from Holland were studied for their circulating antibody to poliomyelitis. The antibody determinations were made by means of a metabolic inhibition test, with fourfold dilutions of serum used. During the course of illness, there was no demonstrable rise in poliovirus neutralizing antibody detected in any patient. It was concluded from the virus-isolation and serologic evidence that infection with any one type of poliovirus had not occurred during the period of illness.

ECHO Virus Type 6 Antibody Studies.—Antibody studies on the Holland patients' serums were carried out in a tissue-culture virus-neutralization test with ECHO virus type 6. Twofold dilutions of serum were tested against 100 TCD_{50} of ECHO virus type 6. Four tissue-culture tubes were employed per serum dilution. The 50% serum dilution end-point (Reed and Muench) was determined, based on readings made 48 hours after all virus control tubes showed definitive cytopathogenic effect. Table 4 summarizes the results obtained. The patients demonstrated rises in circulating antibody to ECHO type 6 virus in a characteristic manner. During the first three days of illness there was little or no demonstrable antibody. Between 5 and 12 days, circulating antibody to the virus appeared, although in modest titer. Seven months after infection, neutralizing antibody was still present. In view of the low order of neutralizing-antibody response, it was considered of interest to do determinations of the antibody content of human gamma globulin to ECHO virus type 6. Human gamma globulin was therefore employed in a neutralization test with one of the Holland agents (no. 14) and also with the prototype ECHO virus type 6. The antibody titers were 32 against each of the viruses. This titer is significant, although of low order.

Comment

Etiological relationship between a common endemic agent and a common clinical syndrome occurring simultaneously in a community is difficult to establish. Proof of such relationship must at the present time depend upon the demonstration of (*a*) association of the agent with clinical cases, (*b*) recovery of the agent from a parenteral site of disease (e. g., cerebrospinal fluid), (*c*) specific neutralizing antibody response during the course of illness, and (*d*) corollary epidemiological evidence within a localized outbreak.

Table 4.—*Neutralizing Antibody Titer Versus ECHO Virus Type 6 in Seven Patients with Aseptic Meningitis in Holland, N. Y.*

Patient No.	Day of Disease: 1	2	3	4	5	6	7	8	9	10	11	12	7-Mo Follow-Up
11			2.5				>64						48
14	<2				11								22
15			<2									9	4
16	<2									27			5
17	<2	<2								14			10
18			<2					27					27
23		<2					32						55

The need for careful evaluation of the role of the orphan viruses in disease is emphasized by the fact that orphan viruses have already been demonstrated to be worldwide in distribution and highly prevalent during the summer months. They have been isolated from fecal material from many areas in the United States[5] and also in Egypt,[1a] the Philippine Islands,[3] Canada,[6] and Sweden.[1b] Two recent surveys have shown that orphan viruses may be common enteric inhabitants. In one survey undertaken by Ramos-Alvarez and Sabin, of 1,566 healthy children in Ohio in the summer of 1953, 25 orphan viruses were recovered from the stools, or an over-all rate of 1.6%.[4a] In the group with the highest recovery rate, namely, children under 10 years of age who came to clinics from families with low income, the recovery rate was approximately 6%. These isolations fell into at least three serotypes. In a three-year survey of a healthy population of children in West Virginia, orphan viruses were recovered by Honig, Melnick, and coworkers in 33 instances from 1,558 stool specimens, a rate of 2.1%.[4b] The highest recovery rate, 11.2%, was from a low socioeconomic area in the four-month period from July through October.

The present demonstration of 7 ECHO 6 viruses among 10 orphan agents recovered from the spinal fluids of patients with aseptic meningitis in western New York is indicative of the invasive properties of this virus. Duncan, Rhodes, and others[6b] recovered two orphan agents, type unidentified, from the spinal fluids of patients with aseptic meningitis. Steigman, Kokko, and Silverberg isolated an orphan agent from the spinal cord of a child with a fatal infection that clinically and pathologically resembled bulbo-spinal poliomyelitis.[7] This agent has recently been identified serologically as ECHO virus type 2.[8] Further attempts to isolate and identify ECHO virus from spinal fluid and nervous tissue will be helpful in establishing the full range of the clinical central nervous system syndromes produced by ECHO viruses.

The Holland patients' neuralizing antibody response, although of a modest order, is in keeping with the low level of antibody for ECHO 6 found in pooled human gamma globulin. This may suggest that under natural conditions of infection the ECHO 6 virus is a poor antigen. However, the absolute level, dependent as it is upon the technique of mensuration, may simply reflect an artefact of the methods employed. With use of an analogous technique, neutralizing antibody titers against poliovirus are approximately tenfold to fiftyfold higher. If one assumes that the pooled gamma globulin represents an approximate twentyfold concentration of antibody, one can presume that the rather low titer of 32 suggests either a small number of adults with sustained high titers of antibody in the population or perhaps a larger number of adults with a barely detectable neutralizing titer. The serologic experience of the population is under study. Utilization of a rise in neutralizing antibody as a diagnostic tool appears to be feasible in this disease, since serum taken prior to the fifth day of disease will in general fail to show antibody and that taken after the fifth day will demonstrate a rise. This is in contrast to the serodiagnosis of poliomyelitis, where the neutralizing antibody has, in the majority of cases, attained maximal titer at the time of recognition of the disease and hospitalization.

The clinical course of illness of the Holland cases was typical of the syndrome known as aseptic meningitis. On admission, symptoms and signs of the patients could not be distinguished on clinical grounds from those of preparalytic poliomyelitis. In retrospect, several features distinguished the Holland cases of aseptic meningitis. First was the apparent high familial incidence of this illness as compared to that usually seen in poliomyelitis. As a corollary, the percentage of manifest versus inapparent disease appeared to be higher than in poliomyelitis. Second, it was noticeable that hot moist packs to the back (prone packs) were not required for more than two or three days, indicating the rapid subsidence of back and hamstring spasm. The significance of the mild muscle weakness and depressed deep tendon and superficial reflexes could not be properly assessed because of lack of controls.

There are already several indications that the association of ECHO virus type 6 with a localized outbreak of cases of aseptic meningitis as occurred in Holland may not be an unusual or isolated occurrence. Studies of a large epidemic of aseptic meningitis in all of western New York in 1955 indicate that such an association was widespread. Simultaneously, at the other end of the state, in Troy, an epidemic of presumably the same illness was studied by Dalldorf.[9] Many strains serologically identical with ECHO virus type 6 were isolated from patients' stools. An outbreak of nonparalytic poliomyelitis in Massachusetts during the summer of 1954 was recently described by Kibrick and others.[10] A high recovery rate of orphan viruses, largely ECHO virus type 6, was made from patients with this illness.

Summary

An outbreak of aseptic meningitis, involving 24 cases, including seven hospitalized children, occurred in Holland, N. Y., population 500, in July, 1955. The predominant clinical symptoms and signs included fever, frontal headache, signs of meningeal irritation, nausea and vomiting, generalized vague pains, minimal transitory muscle weakness, depression of superficial and deep tendon reflexes, and pharyngeal injection. All patients had a pleocytosis, predominantly lymphocytic. ECHO virus type 6 was isolated from 7 stools and 4 pharyngeal specimens of 7 hospitalized children, from 2 of 10 stools and none of 6 pharyngeal specimens of 13 healthy household associates, and from 1 of 3 stools of 3 nonhospitalized patients. All seven hospitalized patients developed a neutralizing antibody response to ECHO virus type 6 beginning on the fifth day of illness. The antibody was still present after seven months. Pooled human gamma globulin had a neutralizing antibody titer of 32 against this agent. In addition, 10 orphan agents were isolated from the spinal fluids of patients in other communities during the course of a subsequent generalized outbreak of seasonal aseptic meningitis in western New York. Seven of these agents were identified as ECHO virus type 6. The high virus recovery rate from stool and pharynx, the epidemiological data, the neutralizing antibody response during the course of illness, and the demonstration of virus

in the spinal fluid of patients are presented as evidence for establishing an etiological role for ECHO virus type 6 in seasonal aseptic meningitis.

Addendum

Since this paper was submitted for publication, Davis and Melnick[11] have reported 24 cases of aseptic meningitis associated with recovery of ECHO virus type 6.

This study was aided in part by contracts with the Communicable Disease Center, U. S. Public Health Service, Atlanta, Ga., and the Erie County (N. Y.) [illegible]

The [illegible] antiserum used in this study was supplied by [illegible] University of Kansas, Kansas City. The Coxsackie prototypic antiserum was supplied by Dr. Gilbert Dalldorf and Miss Grace Sickles, New York State Department of Health, Albany. The 13 ECHO virus prototypes were supplied by the Committee on ECHO Viruses. The human gamma globulin a 16.5% concentration without preservative, was supplied as C-262 by Lederle Laboratories Division, American Cyanamid Company, Pearl River, N. Y.

Drs. Clinton Strong, Holland, N. Y., and A. Wilmot Jacobsen, Buffalo, made available clinical data on their patients for this study.

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METHYLPHENIDATE (RITALIN) HYDROCHLORIDE PARENTERAL SOLUTION

PRELIMINARY REPORT

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• *Methylphenidate hydrochloride was administered in 10-mg. doses by intravenous injection to 164 hospitalized mental patients who manifested sleepiness and other symptoms of overdosage with tranquilizing drugs. The conditions of only 4 of the 164 were refractory to the analeptic effects of the methyphenidate; the other 160 all responded to one, two, or at most three injections by increase in alertness and decrease in side-reactions. Safe and effective dosages were thus determined, and in addition it was found that the improved condition of 151 of the 160 patients could be maintained by giving the methylphenidate solution thrice daily by mouth. A group of 11 chronic, regressed, underactive patients were then treated with intravenous injections of the drug. Three injections of 10 mg. sufficed in every case to cause marked clinical improvement, with increased activity, sudden awareness of surroundings, and other marked changes of behavior. These changes were obtained repeatedly, appeared promptly, were of limited duration, and were not seen after injections of a placebo. They are exemplified in the case histories of two patients who, after 21 and 17 years of extreme inactivity in the hospital, showed dramatic improvement in behavior.*

The psychoanaleptic activity, or stimulating activity on the central nervous system, of orally administered methylphenidate (Ritalin) hydrochloride is well documented clinically.[1] However, clinical information concerning this drug in a new form, methylphenidate (Ritalin) parenteral solution (1%), is needed. This report, although covering our observations made during approximately six months of intravenous administration of this solution to 164 hospitalized mental patients, has been prepared primarily as a preliminary report of findings observed when this solution was administered to 11 chronically regressed, negative, and underactive patients who had been hospitalized for an average of 16 years.

Effects of Drug

In our preliminary evaluation of methylphenidate parenteral solution, we first administered the drug intravenously to patients demonstrating sleepiness, lethargy, tremors, drooling, nasal congestion, conjunctivitis, and Parkinson-like gait produced by too much reserpine, promazine, or chlorpromazine hydrochloride. One hundred six of the 164 patients who received 10 mg. (1 cc.) of the solution intravenously demonstrated improvement of their mental alertness and a

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From the Traverse City State Hospital.

decrease in their side-reactions within 5 to 90 minutes after the injection. Thirty-eight of the 164 responded only after a second intravenous injection of 10 mg. was administered, and 16 of the remaining 20 required 30 mg. intravenously before a clinical change was recorded. The remaining 4 of the 164 showed no change, even though their dosage was raised to 90 mg. intravenously.

After administering 10 to 30 mg. intravenously, as individually needed, three times daily for periods ranging from 24 to 72 hours (three to nine injections), we have been able to maintain the improved condition of 151 of the 160 patients with a comparable dose of methylphenidate given orally three times a day. During the period that the methylphenidate solution was administered intravenously, we recorded no gross change in blood pressure, pulse, or respiration for 160 of the 164 patients. Eight of the 164 became apprehensive and fearful after two to four injections, and 8 others became overactive. These symptoms were alleviated when the dosage was decreased. There was no evidence of serious changes of the skin or tissues at the site of injection, even when extravasation occurred on a few occasions; also there was no evidence of phlebitis. Thus it is indicated that this parenteral solution seems to be well tolerated locally as well as systemically.

From the 164 patients we had acquired a knowledge of indication for use of the drug as well as the proper dosage, safety, and activity of the drug. This prompted us to try a course of therapy with methylphenidate parenteral solution on a group of chronically regressed, underactive patients. Our basic requirements for the patients were simple: a long history of underactivity, no visible reaction when a towel or other object was tossed toward them, and a behavior pattern that indicated they needed help in executing routine daily tasks. Eleven such patients were chosen from another service. An initial intravenous injection of 10 mg. of methylphenidate parenteral solution produced no clinical change in the 11 patients. However, after the second 10-mg. injection and more noticeably after the third intravenous injection of 10 mg. was administered, there was marked clinical improvement in all 11 patients—within minutes. To illustrate the type of patient in this special study and to give examples of our method of administering the solution, two cases are presented.

Report of Cases

Case 1.—A 44-year-old male had been admitted to the Traverse City State Hospital in 1935. He never talked, even when prodded. During the 21 years of his hospitalization he spent practically every waking hour sitting in a chair in the same corner of the same ward without moving. He had to be started to meals, told to go, and helped at the toilet. He needed help in dressing and undressing. He made no visible reaction when a towel was repeatedly thrown to him. At 2:50 p.m. on Sept. 5, 1956, he was given 10 mg. of methylphenidate parenteral solution intravenously. He showed little response. At 2:53 p.m. of the same day he was given a second 10 mg. intravenously. At 2:56 p.m. he caught a baseball when it was thrown to him and soon was playing catch with the nurse. At 5 p.m. he got in line for supper, after going to the toilet without being told to do so. In this short time he demonstrated more voluntary movement and more mental alertness than had been seen during the total of his 21 years in the hospital. This new pattern lasted approximately five hours. On Sept. 9, 1956, the experiment was repeated, with the administration of a single 30-mg. intravenous injection. The response was even more dramatic. In less than five minutes the patient was not only playing catch but was able to examine the ward as if it were his first time to see parts of it, although he had been a patient there for 21 years.

Case 2.—A 41-year-old male had been admitted to the hospital in 1939. During the 17 years that he had been a patient he had never been known to move without help. If his arms or legs were placed in some unorthodox position, they would remain as placed for hours. He needed help and prodding for his every act. At 2:55 p.m. on Sept. 5, 1956, he was given 10 mg. of methylphenidate parenteral solution intravenously. At 2:58 p.m. he was given the second 10 mg. intravenously, and at 3 p.m. he was given another 10 mg. intravenously, thus making a total of 30 mg. At 3:05 p.m. he was playing catch with the nurse and the patient discussed above. His mental awakening lasted approximately four and one-half hours. On Sept. 9, 1956, the experiment was repeated, with the administration of a single intravenous injection of 30 mg. Within five minutes he was playing catch, although he seemed more interested in his hands—as if testing every possible movement.

Comment

On Sept. 12, 1956, the 11 chronically regressed, underactive patients of the special group who had been tested with methylphenidate parenteral solution were tested with placebo injectable solution. Four received as much as 100 mg. (10 cc.) intravenously, without any change from their old pattern. The day after the placebo had been given, the 11 patients were then given 20 to 30 mg. of methylphenidate parenteral solution intravenously. All responded to the drug as they had previously. During the experiments, blood pressure level and pulse and respiration rates were recorded. No changes of significance were recorded.

Therapy with methylphenidate parenteral solution was not continued in 4 of the 11 patients, in order that we may clinically evaluate the activity of other analeptics. This work is in a preliminary stage. However, at this time, none of the other drugs so far tested have produced the dramatic response seen with methylphenidate parenteral solution. Six of the seven patients in whom therapy with orally given methylphenidate has been continued have shown a slow, steady improvement, almost in proportion to the time and retraining they have been given. The improved condition of one patient is maintained only when he is given methylphenidate parenteral solution intravenously or intramuscularly.

Because of its safe, fast action in overcoming most of the so-called side-reactions of the tranquilizing drugs and because of the improvement we have witnessed in chronically underactive patients, the parenteral form of methylphenidate gives promise of opening new doors in our quest to eradicate mental illness. Further studies are recommended.

The methylphenidate hydrochloride used in this study was supplied as Ritalin parenteral solution (1%) by Ciba Pharmaceutical Products, Inc., Summit, N.J.

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GENERALIZED CYTOMEGALIC INCLUSION DISEASE IN NEWBORN INFANTS

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• *Generalized cytomegalic inclusion disease is an intrauterine infection that, in its most serious form, causes symptoms at or soon after birth. The two infants here described had icterus, extensive petechial or ecchymotic hemorrhages, hepatomegaly, splenomegaly, and various laboratory findings indicating a severe blood dyscrasia. One infant died an hour after birth; the other at birth exhibited signs of hemolytic icterus and an anemia that progressed at first but was ultimately controlled. Numerous fresh urine specimens obtained from the second infant during the first two weeks yielded a sediment that, on fixing and staining, exhibited enlarged cells with typical cytoplasmic as well as intranuclear inclusions. The second infant is one of three now known to have survived this disease. The causative organism is a salivary gland virus that probably infects a large proportion of the population subclinically at an early age. The infant who survived was treated with vitamin K intramuscularly, benzathine penicillin G orally, prednisolone, and corticotropin.*

The purpose of this paper is to discuss the clinical picture, etiology, and pathology of cytomegalic inclusion disease as seen in infancy and to describe two cases. One case was diagnosed by the examination of urinary sediment and is the third reported case with recovery of the patient; the second case was diagnosed at autopsy and is typical of the usual past experience with this disease.

Report of Cases

Case 1.—A 2,280 gm. (5 lb.) female was born after eight months gestation terminated by a normal labor and an uncomplicated spontaneous delivery. Both parents were blood type O, Rh positive. At birth the infant was moribund and had severe jaundice, with ecchymoses noted over the back. The head and buttocks appeared abnormally small. A grade 1 precordial murmur was heard, and the cardiac rate was found to be variable. The respirations were irregular, numbering only one to two per minute. The liver was palpable at the iliac crest, and the spleen was similarly enlarged. Ecchymoses became progressively widespread, and the patient's condition deteriorated rapidly, with death occurring one hour after birth. A venipuncture was performed shortly after birth, and bleeding continued for several minutes after death.

The white blood cell count was 80,000 per cubic millimeter, corrected to 38,100; a differential count showed 4 band cells, 18 polymorphonuclear cells, and 78 lymphocytes. The hemoglobin level was 10 gm. per 100 cc. There were 300 nucleated red blood cells per 100 white blood cells, there was marked anisocytosis of the red blood cells, and there were no demonstrable platelets. The infant's blood type was O, Rh positive. The direct Coombs' test was negative, and the Wassermann test was negative. Studies on the mother's blood failed to reveal any abnormal agglutinins. It was impossible to carry out other studies.

Postmortem Examination.—On gross examination the principal findings were slight icterus, widespread petechiae, and marked enlargement of the spleen and liver. Petechiae were present on all the body surfaces; in the mucosa of the esophagus, stomach, ileum, colon, and urinary bladder; in the pleura; and in the kidneys. The heart was normal. The lungs were airless, moist, and heavy. They contained hemorrhages that were particularly prominent in the interlobular septums. The abdomen contained a small amount of icteric fluid, and there was a generalized enlargement and reddish discoloration of the lymph nodes in the mesentery, mediastinum, and retroperitoneal regions. The liver was greatly enlarged to a weight of 156 gm. and extended 5 cm. below the costal margin, as did the spleen, which weighed 52 gm. The kidneys were slightly enlarged, and their cortical architecture was obscured by multiple dark hemorrhagic areas. In the cranial cavity there was a small amount of clotted blood of undetermined origin on top of the tentorium. The brain was of normal size and configuration and contained no lesions on sectioning.

Microscopically the principal lesions were the cells with inclusions and widespread extramedullary hematopoiesis, consisting principally of erythroblastic cells but including myeloblasts and usually accompanied by appreciable interstitial hemorrhage. The inclusions (fig. 1) were of typical type and occurred in greatly enlarged cells. The intranuclear inclusions were very large, ovoid, amphophilic, and rather homogeneous. They were surrounded by halos devoid of chromatin, and the chromatin was condensed upon the distended nuclear membrane. Examples of the irregular basophilic cytoplasmic inclusions were much less numerous than those of the intranuclear inclusions. These inclusions were present in the ducts of the parotid gland; large cells that lay loose in the alveoli of the lungs; the ducts; and other epithelial cells in the portal spaces of the liver, the pancreas (where the islets of Langerhans were particularly involved), tubular epithelium in the kidney, and the pituitary, thymus, and thyroid. One example was found in an endothelial cell in a cervical node. In the brain, several inclusion-bearing cells were present in the neonatal glial mass beneath the ependyma of the lateral ventricles.

Extramedullary hematopoiesis accompanied by significant hemorrhage (fig. 2) was present in the kidneys, liver, and lungs. Hematopoietic tissue without hemorrhage was seen in the spleen, lymph nodes, and thymus and to a slight extent in the epicardium, adrenals, uterus, and pituitary. The liver showed considerable disarrangement in addition to the inclusion cells and the hematopoiesis and hemorrhage. The liver cell cords were poorly developed, and the portal spaces were enlarged and contained irregular and broken cholangioles and an infiltration by lymphocytes and leukocytes. The bone marrow was solidly cellular and contained an excessive proportion of erythroblastic cells but no other abnormalities.

Case 2.—A 2,580 gm. (5 lb. 11 oz.) male was admitted by birth to the newborn service of the University of Virginia Hospital on Oct. 28, 1955. The mother, blood type A, Rh positive, was a primigravida who had experienced an uncomplicated nine-month pregnancy. Labor was complicated by mild preeclampsia. Delivery was facilitated by the use of low forceps. The infant demonstrated the following positive physical findings: (1) a mild degree of icterus of the scleras, a generalized petechial and purpuric eruption, and scaling of the hands; (2) lethargy, although the Moro reflex was active and bilaterally equal; and (3) the spleen palpable 4.5 cm. below the left costal margin and the liver palpable 2 cm. below the right costal margin. On the second day of life a grade 1, high-pitched, systolic, nonradiating murmur was heard at the left sternal border in the fourth and fifth left intercostal spaces.

The initial laboratory studies demonstrated anemia, bilirubinemia, prolonged bleeding time, and poor clot retraction. The bone marrow showed no megakaryocytes, an increased number of nucleated red blood cells, and an over-all decrease in cellular-

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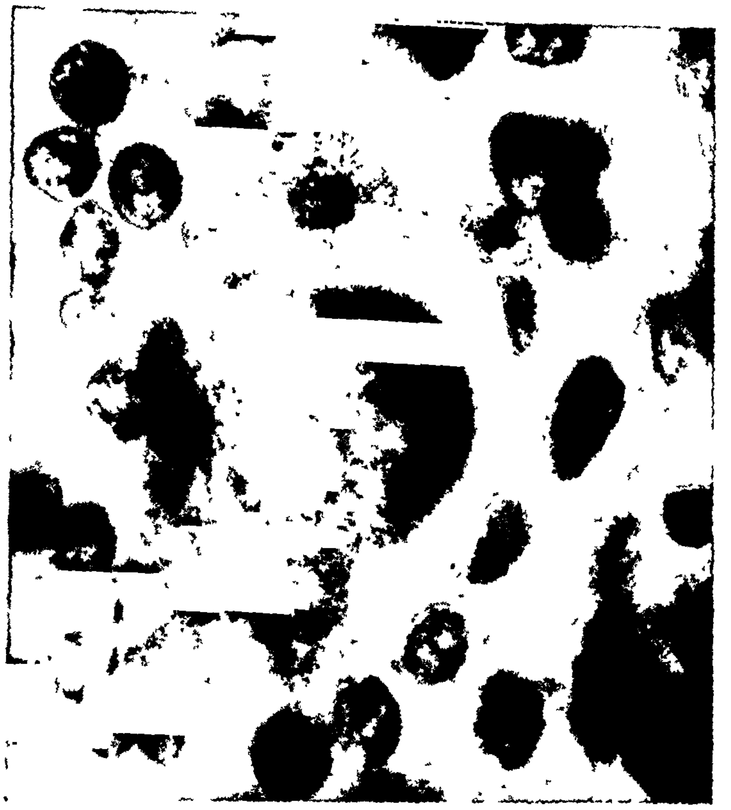

Fig. 1.—Intranuclear and cytoplasmic inclusion bodies of the salivary gland virus type in an enlarged renal tubular epithelial cell (case 1). (× 1,000).

ity. Subsequent blood studies showed progressive anemia, which eventually stabilized, reticulocytosis, and a marked depression of the thrombocytes. Results of other laboratory tests included the following data: Blood type O, Rh negative, Coombs' test negative; Kline test negative, blood cultures negative, and parental blood group incompatibilities absent. Maternal platelet count was 110,000 per cubic millimeter (direct), and studies for toxoplasmosis on the infant and mother were negative. Results of Van den Bergh's test were direct negative and indirect 6 mg. per 100 cc. on Oct. 28, 1955, the indirect being 0.2 mg. per 100 cc. on Nov. 28, 1955. Repeated white blood cell counts and smears were regarded as normal. A urine specimen on Nov. 1, 1955, contained 2 + albumin and 3 to 5 coarse granular casts but was otherwise normal. Stool examination, including trypsin activity, was normal. At birth the coagulation time was 3 minutes, 24 seconds; clot retraction time two hours; and the bleeding time 30 minutes. Thymol turbidity was 4.6 units, and the methylene blue dye test was negative. The platelet counts and serum protein analysis are given in the table. X-rays of the skull and long bones were normal, and funduscopic examination by an ophthalmologist failed to show any abnormalities. Beau's lines were noted on the 16th hospital day.

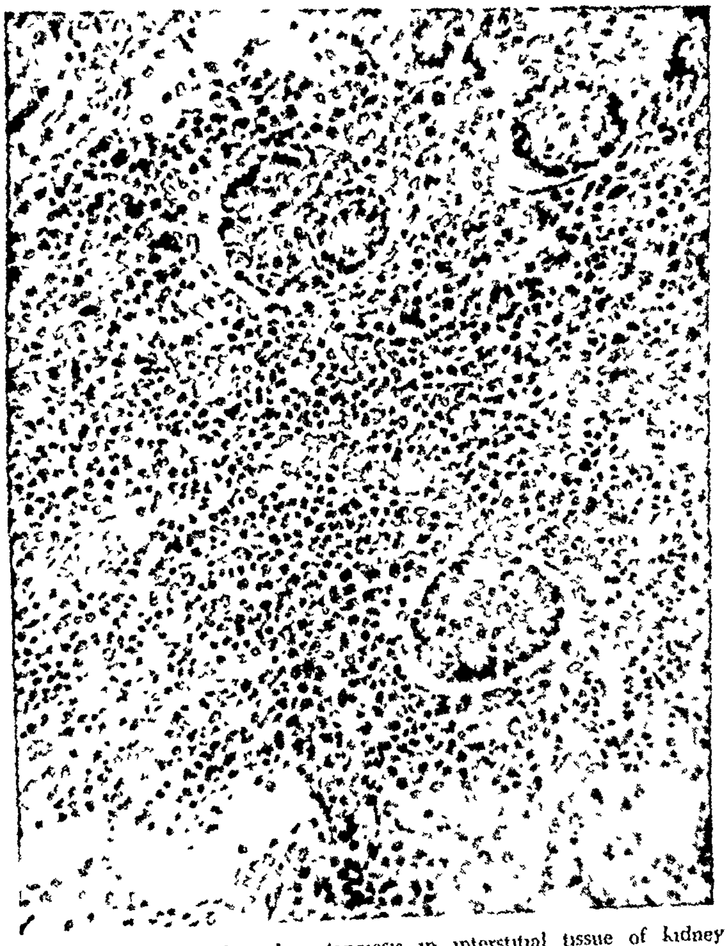

Fig. 2.—Extramedullary hematopoiesis in interstitial tissue of kidney (case 1). These foci were often accompanied by hemorrhage (× 240).

Upon admission to the nursery for newborn infants, the patient was given 5 mg. of vitamin K intramuscularly. Oral administration of benzathine penicillin G (Bicillin), 50,000 units, was begun twice daily. The infant was placed on therapy with prednisolone (Meticorten) given in divided doses of 30 mg. the first day, 20 mg. the second day, and 15 mg. daily thereafter for a period of two months, at which time the steroid therapy was discontinued while corticotropin was administered. During the first two weeks of the 26-day hospitalization, numerous fresh urine specimens were obtained. The sediment was fixed in formaldehyde, and the smears were stained with hematoxylin-eosin and Wright-Giemsa stains. Cells typical of cytomegalic inclusion disease were demonstrated on several occasions (fig. 3). During the three and one-half months of follow-up examinations, clinical progress was satisfactory, without evidence of jaundice and purpura, even though there was some persistence of anemia and diminished production of megakaryocytes on bone marrow examination.

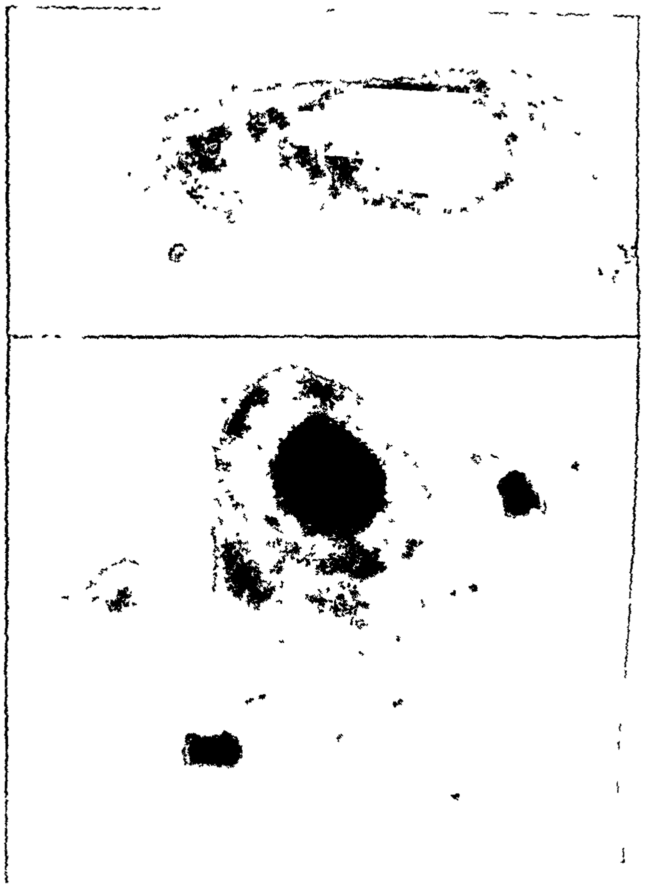

Fig. 3.—Two epithelial cells with intranuclear inclusions from urinary sediment (case 2). The cells were generally sufficiently disrupted that no clear examples of the cytoplasmic inclusions were found (× 1,300)

Comment

History, Etiology, and Clinical Findings.—The salivary gland viruses are the etiological agents of human cytomegalic inclusion disease and of related conditions in many species of animals. These viruses are ubiquitous infectious agents whose names are derived from the early recognition that their characteristic lesions occurred most frequently in salivary glands. The inclusions formed by the action of the viruses were first confused with protozoa, but in 1926 Cole and Kuttner [1] showed that typical lesions in guinea pigs were due to a transmissible and filterable agent. It was then discovered that there were a number of agents that produced the characteristic lesions in various animals but that each strain was species-specific. Except on inoculation into very young animals, the infections produced by these viruses are innocuous.

Knowledge of the human infection has rested on the analogy of the morphological changes in human tissues with those in animal tissues until recently, when Smith[2] successfully propagated the human virus in tissue cultures. Evidence of infection by this virus may be found in tissues under three principal circumstances: (1) incidentally in the salivary glands, (2) in various organs of children and adults who have been ill with other diseases, and (3) disseminated throughout many organs in the newborn infant.

The incidence of the typical inclusions within the salivary glands in routine autopsies of children has been reported as 10 to 32%.[3] This strongly suggests that this virus subclinically infects a large proportion of the population at a relatively young age. The disseminated occurrence of the inclusions in older children and adults has usually been observed in association with other severe diseases and is probably beyond the salivary gland. The generalized disease in the newborn infant appears to be a primary infection by the virus.

Platelet Counts and Serum Protein Analysis of Patient (Case 2) Who Recovered from Cytomegalic Inclusion Disease

	Platelet Count Cu. Mm.
10/28/55	300,000
10/29/55	4,000
11/ 1/55	20,000
11/ 3/55	12,000
11/10/55	16,200
11/14/55	12,700
11/28/55	26,000
12/15/55	68,000
1/ 6/56	79,000
2/ 9/56	114,000
3/ 2/56	63,000
3/ 6/56	58,000

Serum Protein Analysis 2/14/56	Values Found	Normal Values
Total Protein Gm./100 Ml.	6.67	7.35
Serum Protein Pattern (Paper Electrophoresis)		
Albumin, %	52.7	59.4
Alpha 1, %	6.3	6.0
Alpha 2, %	14.4	9.5
Beta, %	15.6	10.7
Gamma, %	11.0	14.4

Although no significant illness has ever been recognized in the mothers of these infants, it is very interesting that the mothers are often primigravida and from relatively isolated rural homes or communities. Such circumstances suggest that this condition results when the mother has an initial, subclinical infection with the virus coincidental with her pregnancy. As no cases have been reported of the occurrence of generalized infantile cytomegalic inclusion disease in more than one child of a given mother and since it appears that most adults have had the infection at some time in their lives, it appears that infection of the mother prior to her pregnancy presents no danger.

The generalized infantile disease may be due to either an intrauterine or a postnatal infection. In the case reported by Gallagher,[4] an infant developed a pulmonary infiltration that progressed to cyst formation in early infancy. On removal of the involved lobe of the lung when the child was 2 months old, typical inclusion bodies were discovered in the bronchial epithelium. This infant survived and apparently has had no recurrence of the disease. Several other cases, such as that of Bacala and Burke,[5] present histories of normal neonatal periods with the subsequent onset of illness during early infancy. Varied symptoms, including vomiting, diarrhea, failure to gain weight, chronic eczema, convulsions, and cyanosis, were described by these authors and they suggested that signs and symptoms might be expected to vary depending upon the organs and tissues most severely damaged by the virus. Cases of congenital brain damage, with calcification, similar to those caused by toxoplasmosis have also been described, and it is suspected that some of these infants may survive.[6]

In the most serious form of the disease, symptoms occur at or soon after birth. This severe generalized infantile disease, as illustrated by the two cases in this report, is apparently due to an intrauterine infection. The signs and symptoms are immediately apparent in the postnatal period, and evidence of the active disease has been seen in stillborn infants. As in hemolytic disease of fetus and newborn infant, the infants are born with some evidence of the disease and develop alarming symptoms in the first few days. The usual signs and symptoms are jaundice, hepatomegaly, splenomegaly, purpura, thrombocytopenia, and hemolytic anemia. Other less frequently described findings are intracranial calcifications, cerebral hemorrhage, convulsions, and cyanosis.[6] Late-occurring symptoms include vomiting, diarrhea, failure to gain weight, and chronic eczema.[5]

The differential diagnosis is that of jaundice, hemolytic anemia, and thrombocytopenia. Diseases that should be considered are hemolytic disease of fetus and newborn infant (Rh, ABO, and other blood incompatibilities), congenital syphilis, spherocytosis, nonspherocytic hemolytic anemia, congenital obstructions of the bile ducts, acute sepsis, toxoplasmosis, and galactosemia, as well as other less common considerations. Fetterman[7] was the first to show that the diagnosis can be made by careful examination of fresh urinary sediment. The finding of tubular epithelial cells with the characteristic inclusions in the sediment is diagnostic of cytomegalic inclusion disease. At the present time, this is the only way to make the diagnosis in the living patient, except by removal of tissue for histological study.

Treatment

At this writing little is known concerning the treatment of cytomegalic inclusion disease. Margileth,[8] in the medical management of the first surviving patient, used cortisone. In our surviving patient steroids were also used. The rationale for steroid therapy was based on recognition of the severe hemolytic features and the knowledge that in other hemolytic diseases cortisone has been helpful. The mechanism of the hemolytic process is not known exactly, but it seems reasonable to assume that, since cytomegalic inclusion disease is caused by a virus, abnormal antibodies might account for the finding of a hemolytic process in these cases. Cortisone has also been used successfully in the treatment of thrombocytopenia, which is a characteristic feature of this disease and which was extremely severe in our patient.

Exchange transfusion has been advocated but not yet reported in the treatment of cytomegalic inclusion disease. The hematological findings represent those of a hemolytic anemia secondary to the viral infection. It would seem that exchange transfusion would be useful in temporarily decreasing the circulating antibody, assuming that an abnormal antibody is present. This form of therapy should be given serious consideration in cases diagnosed in the future. Gamma globulin has been recommended in the treatment of this disease, but we can find no rationale for its use. Antibiotics may be used prophylactically, with no idea of affecting the course of the primary disease process.

Summary

Of two cases of generalized neonatal cytomegalic inclusion disease, in one, a nonfatal case, the diagnosis was made clinically and confirmed by demonstration of inclusions in cells in the urinary sediment; in the other, the clinical and pathological features were typical of most previously reported cases. This disease is an intrauterine virus infection and is characterized by icterus, hemolytic anemia, thrombocytopenia, and other manifestations. At present there appears to be a rationale and clinical evidence for the use of cortisone in treatment of recognized cases. Exchange transfusions might be useful, but specific therapeutic agents are not presently available.

Addendum

The patient in case 1 was seen on Sept. 14, 1956, at which time his physical examination was negative and his weight was 8,504.9 gm. (18 lb. 12 oz.). Both his physical and mental development appeared to be normal.

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CLINICAL NOTES

FATAL AGRANULOCYTOSIS OCCURRING DURING PROMAZINE (SPARINE) THERAPY

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Promazine (Sparine) is 10-(3-dimethylaminopropyl) phenothiazine hydrochloride, one of the newer ataraxic drugs recently introduced into clinical practice. It is chemically related to chlorpromazine, both compounds containing the phenothiazine nucleus. The structure of promazine is the structure of chlorpromazine minus the chlorine atom. Promazine has been used in the management of patients with acute mental disturbances[1] and at this stage is not recommended for patients with chronic conditions. Nevertheless, a clinical trial in such patients was planned. In March, 1956, it was decided to give a course of promazine therapy to 97 patients (50 female, 47 male), all with chronic conditions, who had been hospitalized for from 5 to 25 years. So far as is known, there has been no report in the literature of a case of agranulocytosis resulting from promazine therapy. In order to furnish the first known direct evidence of toxic effects of promazine on the bone marrow, we consider it of interest to report a case of fatal agranulocytosis occurring in a patient during administration of this drug.

Report of a Case

A 57-year-old female was admitted to the psychiatric service on Feb. 25, 1937, with a diagnosis of schizophrenic reaction, paranoid type. The onset of her mental illness was insidious and extended over a period of years. On admission, the physical examination showed nothing essentially abnormal. Psychiatric observation revealed no significant changes over the years. She was seclusive, irritable, hostile, and noisy and did not take part in ward activities. Her speech was rambling, incoherent, and at times difficult to understand because of a marked German accent. She had hallucinosis. The patient had not previously received any of the ataraxic drugs, and there was no history of any convulsive disorders. Blood studies prior to promazine therapy showed a white blood cell count of 8,200 per cubic millimeter, a hemoglobin level of 15.4 gm. per 100 cc., and a hematocrit value of 42%. The total serum bilirubin level was 0.32 mg. per 100 cc.,

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with direct 0.1 mg. and indirect 0.22 mg. Urinalysis (not a catheterized specimen) showed a specific gravity of 1.022 and was negative for acetone, albumin, and sugar, with an occasional white blood cell being seen on the microscopic examination. X-ray of the chest was negative.

Promazine therapy was started June 4, 1956. The initial dosage was 100 mg., 200 mg., and 400 mg. for the first, second, and third days respectively. After the third day, the dosage was increased by 100 mg. per day each week until a total daily dosage of 1 gm. was reached (July 16, 1956). All medicaments were given by mouth and in divided doses three times daily. On July 3, 1956, the three times daily dosage was changed to four times daily. Temperature, pulse and respiration rate, and blood pressure were taken daily during the first two weeks of therapy and showed no marked variation from normal. The patient's mental status showed little, if any, improvement at this period of treatment.

On July 6, the 31st day of promazine therapy, blood studies revealed a white blood cell count of 3,800 per cubic millimeter, with a differential count of 60% neutrophils and 40% lymphocytes. The hematocrit value was 38%. The patient's temperature was normal, and physical examination revealed no evidence of infection, sore throat, or ulceration of the mouth. No enlarged lymph nodes were palpable. The treatment with promazine was continued, with daily inspections and observations of the patient.

On July 20, the patient was noted to be unusually confused and unsteady on her feet and was reported to have fallen in the bathroom late in the afternoon. Her temperature was normal, and physical examination revealed no positive findings. On July 21, the 46th day of therapy, the patient had a petit mal seizure lasting two minutes. There was no injury. At this time there was a rectal temperature of 102.8 F (39.3 C). The patient was responsive and there were no positive physical findings. She was given 10 grains (0.6 gm.) of aspirin and fluids by mouth.

On July 22, the patient's temperature in the morning was up to 103 F (39.4 C). The only positive physical finding was fecal impaction. An enema was given. The fluid intake for the previous 24 hours had been 1,590 ml., and the output was 400 ml. Promazine was withdrawn. At this time, medical consultation was requested, and the patient was transferred to the medical and surgical branch in the afternoon. Physical examination at the medical and surgical branch revealed these positive findings: scleras, slightly icteric; lungs, dulness at left base with increased breath sounds and a few coarse rales; heart, pulmonic second sound greater than the aortic second sound, with a loud grade 2 systolic murmur in all areas; and abdomen, protuberant, slightly tense, no palpable organs, and fecal impaction. The neurological examination revealed active tendon reflexes bilaterally. There was extreme weakness in both legs, with hypotonia. The patient did not appear acutely ill.

A roentgenogram of the chest was essentially normal, and urinalysis showed a specific gravity of 1.004, traces of albumin, an occasional hyalin cast, white blood cells, and many bacteria. A blood culture was taken and was reported sterile. A blood cell count showed 575 white blood cells per cubic millimeter, with 90% lymphocytes. The hematocrit value was 33% and the hemoglobin level 9.3 gm. per 100 cc. A throat smear and culture showed beta-hemolytic streptococci, gamma streptococci, nonhemolytic micrococci, and Escherichia coli.

On July 23, the white blood cell count was 600 per cubic millimeter, with no mature neutrophils, and a sternal puncture was done for a bone marrow study. The bone marrow showed complete maturation arrest of the granulocytic series, with only myeloblasts seen. There was an increase in the mononuclear series, such as lymphocytes, plasma cells, and reticular cells. Urinalysis showed a specific gravity of 1.007 and was positive for hemoglobin. Microscopic examination revealed increased cylindruria. The patient showed increased inability to move her legs. There were small areas of ecchymosis in both eyes. A diagnosis of agranulocytosis due to drug reaction was made.

Medical treatment consisted of the intramuscular administration of tetracycline (Achromycin), 200 mg. every four hours; procaine penicillin, 600,000 U.S.P. units once daily; procaine penicillin for aqueous injection, 300,000 U.S.P. units every two hours; and cortisone, initially 200 mg. administered intramuscularly, then 100 mg. every eight hours. The patient was given 40 units of corticotropin (ACTH) with the first dose of cortisone. Because of the decrease in red blood cells, 500 ml. of blood was administered July 23. One concentrated, salt-poor unit of liquid normal human serum albumin (25 gm. albumin in 100 ml.) was also given. The patient's intake and output of fluid was measured, and supportive fluid was administered intravenously.

On July 24, cortisone, 100 mg. three times daily, was given, and on July 25 the cortisone was decreased to 40 mg. every six hours. At this time, clinical jaundice was evident and agranulocytosis of the oral cavity and oropharynx was noted. The abdomen showed moderate distention on the morning of July 26. That afternoon acute pulmonary edema with auricular fibrillation developed, and the blood pressure fell to 60/40 mm. Hg. The patient for the first time appeared critically ill. She was digitalized with lanatoside C (Cedilanid). Oxygen nasally and methoxamine (Vasoxyl) hydrochloride, 1 ml. intravenously and intramuscularly, were administered. There was complete renal shutdown, and the blood pressure failed to rise above 60/40 mm. Hg. In the early morning of July 27, the patient died.

Results of additional laboratory studies during her course in the hospital were as follows. On July 24, total bilirubin level was 5.54 mg. per 100 cc., with direct 3.99 mg. and indirect 1.55 mg., thymol turbidity, 4 units (Shank-Hoagland); cephalin flocculation, negative in 24 hours; serum alkaline phosphatase, 5 Bodansky units; and prothrombin time, 16.9 seconds (control) and 14 seconds. The white blood cell count was 350 per cubic millimeter in the morning and 125 in the afternoon, with 90% lymphocytes in both counts. The hematocrit value was 32% and the hemoglobin level 10 gm. per 100 cc. Urinalysis showed numerous granular casts, 1+ albumin, and 2+ sugar. On July 25, the total bilirubin value was 10.6 mg. per 100 cc., with direct 8.4 mg. and indirect 2.2 mg. The white blood cell count was 450 per cubic millimeter, with 50% lymphocytes; hemoglobin level 8.9 gm. per 100 cc.; and hematocrit value 29%. The nonprotein nitrogen level was 47 mg. per 100 cc. on the morning of July 26. The gross findings at autopsy were pulmonary edema and atelectasis, acute ulcerative colitis, fatty metamorphosis of the liver, and agranulocytosis.

Comment

Apparently most of the ataraxic drugs are capable of depressing the bone marrow when used in sufficient dosages and over long periods of time. The advisability of frequent blood cell counts during the administration of these ataraxic drugs cannot be overemphasized.

Summary

A fatal case of agranulocytosis occurred in a patient on the 48th day of administration of promazine (Sparine). The dosage had been instituted at 100 mg. per day and reached a maximum of 1 gm. per day in four divided doses over a 42-day period.

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Improvements in Cancer Survival Rates.—The Connecticut Cancer Record Register has information on 75,494 cancer cases diagnosed from 1935 through 1951. Follow-up information reveals that the outlook for survival is improving for some forms of cancer. Marked increases in five-year survival rates were observed for patients with cancers of the large intestine, rectum, cervix, corpus, prostate and endocrine glands. Both earlier case finding and more effective utilization of available therapeutic technics apparently were factors in increasing the proportion of cancer patients alive five years after diagnosis. Effective use of technics has had a more measurable effect in recent years. Further increase in survival must be predicated on research for better diagnostic and therapeutic methods.—M. H. Griswold, M.D., S. J. Cutler, M.A., and H. Eisenberg, M.D., *The New England Journal of Medicine*, June 7, 1956.

COUNCIL ON FOODS AND NUTRITION

Report to the Council

The following paper was presented at the symposium, "Some Inorganic Elements in Human Nutrition," in Nashville, Tenn., April 4, 1955. This symposium was sponsored jointly by the Nashville Academy of Medicine, the Vanderbilt University School of Medicine, and the Council on Foods and Nutrition. This report is the final of the series, others of which appeared in The Journal *April 21, June 9, Sept. 15, and Nov. 10, 1956.*

Philip L. White, Sc.D., *Secretary.*

PHYSIOLOGICAL BASIS OF POTASSIUM THERAPY

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Rational treatment of disturbances of the body potassium level is based on the physiology of water and electrolytes. Beginning with Ringer's studies of the effects of electrolytes on the heart, numerous investigations have indicated that the activity of all cells is altered by changes in the concentration of the potassium surrounding the cells. High plasma concentrations exert their most important effect on the heart, because arrhythmia and heart block are produced at plasma potassium concentrations of 8 to 10 mEq. per liter.[1] A flaccid paralysis of skeletal muscle has been observed at high concentrations in some patients with advanced renal failure. The paralysis resembles that seen with low plasma potassium levels except that the electrocardiograms are characteristic of those of patients with potassium intoxication. The high-peaked T waves are the earliest electrocardiographic alterations, but absent P waves, spreading QRS complexes, and more advanced disturbances develop later.

When the potassium concentration in plasma is low, a patient's first complaint is usually lassitude and weakness. The electrocardiograms often show flat T waves that may be inverted. Little evidence of cardiac failure is present in mild deficiency, but when potassium deficiency is severe and prolonged, circulatory failure and myocardial necrosis occur. The skeletal muscles show diminished tone, weakness, and, under certain circumstances, flaccid paralysis identical with that described in familial periodic paralysis. The weakness is usually more pronounced in the lower extremities, but the muscles of respiration may be sufficiently involved to interfere with their functions. The smooth muscles also show decrease in tone, producing intestinal and gastric distention, nausea, occasionally vomiting, and finally paralytic ileus. Indeed, potassium deficiency must always be considered a possible cause of paralytic ileus, although other disturbances produce the same picture. The paralysis in both smooth and skeletal muscles is apparently caused by a failure of myoneural conduction that is readily reversed by an increase in serum potassium concentration. Potassium also alters other neural reactions. Certain patients with low serum calcium levels do not have tetany when the serum potassium level is low, but tetany is manifest when potassium concentration rises to normal.[2]

In a study made in 1945, the implications of the changes in muscle composition observed in rats were discussed.[3] On the basis of these experiments it was possible to deduce many of the clinical states of potassium deficiency in patients, which subsequent studies have demonstrated. The quantitatively important alterations in potassium in the body are accounted for by changes in potassium in muscle. There is no evidence of increased storage of potassium in cells except for the slight rise that accompanies an increase in serum concentration. This increase in cell potassium levels does not persist when normal plasma concentrations are restored. A decrease in the muscle potassium level may be great, but it is not necessarily accompanied by decreases in serum concentrations. As a result of diets low in potassium, muscle potassium levels may decrease to half the normal value.[4] Usually about two-thirds of the decrease is replaced by an increase in intracellular sodium. This is equivalent to a loss of about 25 mEq. of potassium per kilogram and an increase of intracellular sodium of about 17 mEq. per kilogram of body weight. Clinical studies indicate that essentially the same changes occur in patients. Evaluation of the clinical states is closely related to the experimental studies.

The potassium content of the cell is primarily dependent on the cell's structural and metabolic integrity. It is not known by what mechanism the cells maintain a high concentration of potassium and a low concentration of sodium while surrounded by extracellular fluids with a low potassium and a high sodium concentration. Water is exchanged rapidly between extracellular and intracellular fluids, but the rate of net exchange of sodium and potassium is somewhat limited. It is clear that potassium leaves and sodium enters the cells when cellular metabolism ceases. A more limited exchange of this type probably occurs when metabolic processes are impaired. Anoxia and insulin deficiency are examples of this type of altered exchange that can be reversed.

The therapeutic administration of potassium first requires treatment that restores normal cellular metabolism as far as this is possible. In shock and dehydration, replacing deficits of water and extracellular

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electrolytes is the first step in treating potassium deficiency. Although restoration of extracellular water and electrolytes is the most important means of correcting the circulatory failure of dehydration and deficit of sodium and chloride, transfusions make this therapy definitely more effective in experimental animals and patients. In hemorrhagic and oligemic shock, transfusions are essential. Likewise, insulin is necessary in diabetic coma in order to facilitate the uptake of potassium by cells depleted of this ion. Administration of water, sodium, and chloride is equally important in patients who have suffered large losses; administration of oxygen is indicated in some anoxic patients. These measures that restore cellular metabolism should be carried out before the administration of potassium is started.

Rapid restoration of cellular metabolism in a patient with large cellular deficits of potassium may lead to rapid transfer of extracellular potassium to the cells. Consequently, symptoms of low concentration of potassium in serum are likely to develop rapidly. If renal function is good, the administration of potassium may be started early, but it should be started slowly and in anticipation of the decrease in serum potassium concentration. Owing to the particularly rapid restoration of cell metabolism in diabetic coma, frank symptoms of potassium deficiency are especially likely to develop in patients treated without potassium at the time when the effects of insulin appear. Patients in alkalotic states with potassium deficiency are also likely to develop symptoms of hypokalemia because alkalosis increases the tendency to transfer potassium from extracellular to intracellular fluids. In diabetic coma, skeletal muscle weakness and paralysis have been observed, whereas in alkalosis, intestinal distention, vomiting, and paralytic ileus are more frequent. In other types of acidosis with potassium deficiency, a decrease in serum potassium concentration during treatment is likely to develop more slowly. The reason for this is that, initially, the serum potassium concentration is likely to be somewhat high, and transfer of potassium from extracellular to intracellular fluids is retarded by acidosis. If sodium bicarbonate or its equivalent is given to increase rapidly the plasma bicarbonate level, a decrease in serum potassium concentration is likely to be accelerated.

These statements are based on clinical observations and experimental studies. When muscle is placed in Ringer's solution with a given potassium concentration, a high pH of this solution leads to transfer of potassium to the cells while a low pH produces the opposite effect. This observation has been confirmed in nephrectomized dogs receiving injections of ammonium chloride or sodium bicarbonate. In otherwise normal dogs, production of metabolic acidosis and alkalosis demonstrates an inverse relationship between serum pH and serum potassium concentration that is not explained by a change in total body potassium.[5] In dogs previously depleted of potassium, the same inverse relationship is manifest; however, the serum potassium concentrations remain somewhat lower. As would be anticipated, potassium tends to enter the cells as serum potassium concentration rises, and vice versa. This reaction is more or less independent of the shifts accompanying changes in pH.

The clinical implications of these observations are reasonably clear. Serum potassium concentration reflects the changes in serum pH and the concentration of potassium in cells. The serum potassium concentration is likely to be low in alkalosis even if the cell potassium level is relatively normal but especially low when cellular potassium deficiency is present. In alkalosis, serum potassium concentration is not likely to be high unless renal function is impaired and the cell potassium level is relatively normal or unless disturbances in cellular metabolism have developed. In acidosis, serum potassium concentration is likely to be normal or high despite cellular deficits. Low serum potassium concentrations in acidosis usually indicate considerable deficits of intracellular potassium. Disturbances in cellular metabolism and renal function must also be considered in evaluating potassium concentration in acidosis.

Renal response to respiratory changes in acid-base equilibrium tends to exaggerate the changes in plasma concentration produced by the alteration in carbon dioxide tension. In respiratory acidosis, carbonic acid donates hydrogen ions to buffers, thereby forming undissociated weak acids and raising serum bicarbonate. The kidneys further increase bicarbonate concentration by excreting hydrogen ions. The process is, in effect, an exchange of plasma chloride for bicarbonate of the glomerular filtrate. In this process, the muscle potassium level is well maintained.[6] In respiratory alkalosis, the exchange for sodium of hydrogen ions freed from undissociated weak acids decreases plasma bicarbonate. The kidneys exaggerate the decrease in bicarbonate by retaining hydrogen ions. This is accomplished by exchanging plasma bicarbonate for chloride of the glomerular filtrate. It is not known whether serious deficits of potassium develop in respiratory alkalosis. In any case, replacement therapy is seldom indicated, since the kidneys readily restore normal body electrolyte balance when carbon dioxide pressure becomes normal.

In metabolic acidosis, the normal kidneys tend to restore normal extracellular concentrations if sufficient sodium, potassium, chloride, and water are available. The fundamental operation that restores a low serum bicarbonate value is the excretion of hydrogen ions. Experimental acidosis caused by administration of hydrochloric acid to dogs is corrected first by excretion of the excess of chloride with sodium and then potassium. The excess of chloride is reduced, but deficits of sodium and potassium are likely to develop; hydrogen ions are not excreted, and bicarbonate concentration is not restored. Only after 1 or 2 days are sufficient ammonium ions formed to conserve sodium and potassium and to excrete hydrogen ions effectively. These observations indicate that in metabolic acidosis abundant sodium and potassium are required for renal compensation. The experiments also show that deficits of potassium as well as of sodium are likely to develop. The changes in body composition are not confined to extracellular fluids.

In metabolic alkalosis, the normal kidneys also tend to restore normal plasma concentrations if sufficient sodium, potassium, chloride, and water are available. The fundamental operation is retention of hydrogen ions. This is accomplished, in effect, by excretion of bicarbonate or organic acids with sodium and potassium. Metabolic alkalosis is usually accompanied by a relative or absolute excess of sodium in the body. Accordingly, the renal compensation is only likely to produce deficits of potassium. The course of events is well illustrated by experiments on rats given large loads of sodium bicarbonate and variable amounts of potassium chloride.[7] Alkalosis, which developed only when the intake of potassium was low, was always accompanied by a decrease in muscle potassium and an increase in intracellular sodium. Apparently excretion of a certain amount of potassium is necessary to preserve plasma chloride concentrations and to prevent alkalosis. These observations fit in well with clinical experience, which shows that metabolic alkalosis is not corrected despite an abundant excretion of sodium and chloride when potassium deficiency develops.[8]

The plasma bicarbonate concentration varies directly with intracellular sodium and inversely with the muscle potassium level in experimental rats. Clinical observations fit in well with these observations if due attention is paid to the experimental conditions. Metabolic acidosis was produced by removal of sodium bicarbonate by peritoneal exchange and maintenance of rats on a diet containing abundant potassium and chloride but no sodium. Metabolic alkalosis was produced by peritoneal exchange of body chloride for bicarbonate. The rats received a diet abundant in sodium and potassium but no chloride. Potassium deficiency was produced by injections of desoxycorticosterone acetate in rats on a low-potassium diet with an abundance of sodium chloride. Sufficient time was allowed in all experiments to permit renal adjustment to the experimental conditions. Deficit of chloride and potassium resulted in essentially the same changes in the muscle and serum, that is, metabolic alkalosis, high serum bicarbonate values, and low chloride concentrations with low muscle potassium and high intracellular sodium levels. Deficit of sodium bicarbonate resulted in metabolic acidosis and low intracellular sodium and high muscle potassium concentrations. Changes in the metabolic alkalosis and potassium deficiency are frequently met in clinical medicine; however, metabolic acidosis is not often seen in patients when an abundance of potassium is available.

Protein milk produces metabolic acidosis accompanied by retentions of potassium and chloride.[9] Muscle potassium concentration is probably high in such cases. Acidifying salts may have a similar effect if the intake of potassium is high. Usually the losses of electrolyte, which produce metabolic acidosis, result in deficits of potassium as well as in deficits of sodium and chloride. Diminished intake of potassium and losses of this ion in diarrheal stools produce considerable deficits of potassium, sodium, chloride, and water.[10] In addition to the losses of bicarbonate with sodium in the stools, the extracellular bicarbonate level is reduced by loss of bicarbonate with potassium in the stools. The cellular deficit of potassium is partially replaced with extracellular sodium. Similar changes in body composition occur in diabetic coma. Organic acids are excreted with potassium as well as with sodium. Although some of the reduction in plasma bicarbonate is accounted for by displacement of bicarbonate by ketone acids, a major part is usually caused by excretion of bicarbonate with sodium and potassium.

The importance of the changes in body composition is brought out in studies of experimental alkalosis with potassium deficiency in rats. The exchange of ions between extracellular and intracellular fluids, as well as by renal regulation, explains the restoration of normal acid-base equilibrium by administration of either potassium chloride or potassium bicarbonate with no external source of sodium.[7] With the administration of potassium chloride, the exchange between extracellular and intracellular fluids may be depicted as follows: 3 KCl is added to the extracellular fluids; 3 K^+ enter the cells in exchange for 2 Na^+ and 1 H^+. The H^+Cl^- reacts with $NaHCO_3$ to form CO^2, H^2O, and Na^+Cl^-. Consequently, bicarbonate concentration is restored without excretion of bicarbonate by the kidneys being required. With administration of potassium bicarbonate, the same exchange at the membrane takes place; 2 $NaHCO_3$ and 1 H_2CO_3 are formed in extracellular fluids. Bicarbonate must be excreted by the kidneys in order to restore normal acid-base equilibrium. Chloride concentration rises (despite no external source of chloride) because extracellular volume decreases, as indicated by a decrease in body weight.

The foregoing description of the exchange between extracellular fluids and muscle indicates that the reverse exchange occurs during the development of metabolic alkalosis. In other words, the muscle cells in metabolic alkalosis have received an excess of hydrogen ions that is as great as the deficit of hydrogen ions in extracellular fluids. The excess of hydrogen ions probably produces little change in cell pH since protons from the hydrogen ions would form undissociated weak acids or possibly weak bases from amino compounds. Potassium is apparently necessary for the renal compensation of metabolic alkalosis. This observation is confirmed in those patients with metabolic alkalosis who fail to respond to administration of saline solution unless potassium is also available.[11]

Metabolic acidosis has not been studied in similar detail; however, it is clear that large doses of sodium bicarbonate are required to restore bicarbonate concentration in metabolic acidosis, not because the deficits of sodium bicarbonate are this great in extracellular fluid but because, as the result of a potassium deficiency, a large part of the injected sodium ion enters the cells in exchange for the hydrogen ion. Since the extent of this transfer cannot be predicted in patients, the calculation of the dose of sodium bicarbonate required to restore acid-base equilibrium has no sound physiological basis. The cellular deficit of cations should be replaced with potassium. In general, acidosis accompanied by dehydration should be treated by replacing extracellular water and electrolytes by a solution resembling extracellular fluids, such as Hartmann's Ringer lactate. Simultaneously, or as soon as renal function and cellular metabolism are adequate, potassium should be given in amounts that adequately cover normal expenditure and replace some of the deficits. It is seldom necessary to give more bicarbonate than that contained in this solution; however, 4 mM. of sodium lactate per kilogram of body weight (25 ml. of 0.16 M) may safely be given in severe acidosis of this type.

Schwartz and Relman[12] have described persons with severe potassium deficiency that resulted from repeated use of cathartics. These patients did not develop alkalosis. The renal function was altered; hyposthenuria and moderate reduction in glomerular filtration were demonstrated. Renal function did not return entirely to normal over a period of several months. The authors postulated that prolonged potassium deficiency produces renal changes that are not rapidly reversed. The renal disturbances developing in some patients under prolonged Sippy treatment may be of this type.

Schwartz has reviewed the literature on potassium in relation to the kidneys.[13] The excretion of potassium increases when serum concentration of this ion increases. Both acidosis and alkalosis increase potassium excretion; administration of acetazolamide leads to prompt excretion of potassium. Urine with a high level of sodium usually has a high potassium level. The mercurial diuretics produce alkalosis that may or may not be accompanied by deficits of potassium. Desoxycorticosterone, aldosterone, cortisone and other corticosteroids, adrenotropic hormone, and activation of the adrenal cortex increase urinary potassium levels. When oliguria develops in renal failure or when extrarenal factors such as shock and dehydration are present, potassium tends to be retained and toxic levels may be reached. Nevertheless, potassium excretion is usually well maintained in advanced renal insufficiency as long as the urine volume is high. Indeed, symptoms of potassium deficiency have resulted from renal losses in some patients with hyposthenuric renal insufficiency.

The stools normally contain moderate amounts of potassium. Losses of potassium in patients with infantile diarrhea are as great as 17 mM. per day as compared to 2 mM. per day in healthy infants. Stool losses and decreased intake are largely responsible for potassium deficiency in diarrhea. In one study, stool concentration of potassium was reported to be about 57 mEq. per liter in fed patients; during the recovery of patients not fed, the potassium concentration in stools was about 40 mEq. per liter.[10] One patient with voluminous stools containing a large quantity of sodium and chloride was reported to be excreting only 6 mEq. of potassium per liter. When isotonic sodium chloride solution is placed in the colon, potassium concentration rises to about 40 mEq. per liter as sodium chloride and water are absorbed.[14] This finding suggests that the loss of potassium will be high if watery stools remain long in the colon but low if the fluids from the small intestine are rapidly passed through the colon. As was pointed out by Gamble,[15] death from diarrhea may be considered to result from accumulating deficits. It can be calculated that serious water deficits appear first when there is no replacement. If water is restored, deficits of sodium and chloride become serious after only a slightly longer period. If water, sodium, and chloride are restored, potassium deficits are serious after a slightly longer period.

Treatment of infantile diarrhea involves the restoration of water and electrolytes as well as the restoration of normal stools. In a report mentioned earlier, the average deficits were 125 gm. of water, 9 mM. of sodium chloride, and 12 mEq. of potassium per kilogram of body weight. A postacidotic state after the treatment of infantile diarrhea was described by Rapoport and associates.[16] A decrease in serum concentration of phosphorus, potassium, and calcium was frequent, and failure to recover was attributed to hypocalcemic tetany in many cases. Although I have observed hypocalcemia occasionally in patients recovering from infantile diarrhea, this finding has been rare when potassium as well as sodium salts have been used. A possible explanation of the contradictory experiences is that in normal rats administration of sodium chloride and sodium bicarbonate does not produce hypocalcemia, but the same salts reduce serum calcium concentration in rats previously depleted of potassium. Potassium deficiency alone does not reduce calcium concentration. It is believed that a disturbance in the regulation of extracellular calcium concentration develops when sodium concentration is rapidly increased in the presence of potassium deficiency. To the extent that hypocalcemia explains the postacidotic state, this hypothesis indicates that tetany of this type is an iatrogenic disorder resulting from the administration of too much sodium bicarbonate to patients deficient in potassium. Presumably, early administration of potassium prevents this disturbance.

The association of alkalosis and profuse watery stools in congenital alkalosis with diarrhea is a rare condition.[17] The fluid in the small intestines is normal and food is well absorbed; however, the stools contain large volumes of water, more chloride than sodium, and a considerable amount of potassium. The deficit of chloride accompanying marked elevation of the serum bicarbonate concentration is explained by stool losses, since the urine is practically devoid of chloride.

Prolonged fasting may induce marked alkalosis and potassium deficiency. Some patients with anorexia nervosa exhibit this phenomenon.

The treatment of potassium deficiency is essentially the same in persons of all ages. Deficits should be estimated in milliequivalents per kilogram of body weight and are unlikely to be greater than 17 mEq. per kilogram. It is usually safe to give 3 mEq. per kilogram per day together with the appropriate amounts of fluid to cover normal and abnormal expenditure and to restore initial deficits of sodium and chloride. The total fluid requirements in infants are sufficient so that this amount of potassium can be given at a concentration of 25 mEq. or less per liter. In adults, the appropriate amounts of fluid are such that concentration of potassium would have to be 60 mEq. per liter in order to supply this amount. It is desirable not to exceed a concentration of 40 mEq. per liter of fluid injected into the veins. The estimated amount of potassium for 24 hours may be injected more rapidly but not in less than 4 hours. For severe deficiency, somewhat larger doses may be given, but their effects should be carefully observed by electrocardiography, measurement of serum concentrations, and clinical observation of the patient. The amounts of potassium that can be given safely are such that it takes 4 to 6 days to replace large deficits.

Total fluid requirement should be estimated as 150 ml. per 100 calories metabolized. This practice takes into account the different rates of expenditure of water that accompany different metabolic rates in infants and adults and other factors altering total metabolism. Total metabolism is usually about 1,000 calories per square meter of body surface, and fluid requirement about 1,500 ml.; however, in newborn infants who have not been fed, the total metabolism is low—about 60% of the usual amount per square meter. The fluid requirement after operations in the newborn infant is not low per unit of metabolism. It is lower than the usual amounts calculated per kilogram of body weight or per unit of surface area.

The expenditure of potassium when all fluids are given parenterally varies from 1 to 3 mEq. per 100 calories metabolized—usually 20 to 30 mEq. per square meter per 24 hours. Even when there is no deficit of potassium, these amounts should be given in order to prevent deficiency.

A suitable mixture for replacement of fluid removed by gastric suction is sodium chloride solution of about one-half isotonic strength and 40 mM. of potassium chloride (3 gm.) per liter in a 2.5% dextrose solution. In most cases of metabolic alkalosis, the deficits of sodium chloride are replaced by 20 to 40 ml. per kilogram of isotonic sodium chloride solution. To this, the therapeutic amount of potassium chloride should be added.

Often electrolyte therapy can be oral when food cannot be taken. The requirements of water, sodium, chloride, and potassium are the same as when all fluids are given parenterally. This means that the normal expenditure of 3 mM. of sodium chloride and 2 mEq. of potassium per 100 calories metabolized would be given in 150 ml. of water. It is advisable to prescribe definite mixtures such as 1 gm. each of sodium chloride, sodium bicarbonate, and potassium chloride in a liter or quart of a 5% glucose solution. Such a solution has made it possible to handle practically all cases of mild infantile diarrhea without administering fluids parenterally. Use of the mixture permits the period of parenteral administration of fluid to be shortened. The solution has been useful in the postoperative care of infants and children and is appropriate in both acidosis and alkalosis; there is no reason why it should not be effective in similar conditions in adults. I have found it more convenient and safer to use a mixture of definite composition manufactured for this purpose (Lytren). This mixture contains electrolytes sufficient to replace moderate deficits of sodium, chloride, and potassium and to provide for a moderate increase in expenditure. Such mixtures should be prescribed in definite amounts suitable to cover normal water expenditure. Additional water may then be added when expenditure of water is high.

Summary

Potassium deficiency is likely to develop in acidosis or alkalosis when there is prolonged diarrhea or prolonged parenterally given fluid therapy without potassium. Fasting may induce deficiency. The cortical hormones increase the amount of potassium in the urine. Renal function is altered by alkalosis so that potassium deficiency is likely to appear. Potassium deficiency alters renal function so that alkalosis appears or persists. The excretion of loads of anions with potassium is part of the cause of potassium deficiency in acidosis. Potassium intoxication may develop when oliguria occurs in renal disease or when renal function is impaired by extrarenal factors such as shock or dehydration. Administration of potassium with suitable mixtures of sodium, chloride, and glucose in water is relatively safe if certain rules as to dose and rate of administration are followed. Renal function should be good and the circulatory failure of shock overcome. The chief contraindication to potassium therapy is renal failure with oliguria and untreated adrenal insufficiency.

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COUNCIL ON PHARMACY AND CHEMISTRY

NEW AND NONOFFICIAL REMEDIES

Monographs and supplemental statements on drugs described here and in subsequent editions of New and Nonofficial Remedies are based on the evaluation of available scientific data and reports of investigations. Applicable commercial names for preparations of evaluated drugs are listed at the end of monographs and parenthetically in the text of supplemental statements; additional commercial names of which the Council is informed will be included with subsequently published supplemental statements and annual editions of New and Nonofficial Remedies. H. D. Kautz, M.D., *Secretary.*

Topical Use of Prednisolone

The Council has evaluated the topical use of prednisolone (Meti-Derm) for the local management of dermatoses susceptible to gluco-steroid therapy. On the basis of currently available evidence, the Council concluded that the drug, incorporated in a suitable dermatological vehicle, is effective in ameliorating cutaneous manifestations of acute and chronic dermatoses that have an allergic or inflammatory basis and are associated with pruritus. These include such conditions as contact dermatitis, various forms of atopic dermatitis, seborrheic dermatitis, nonspecific anogenital pruritus, and lichenified pruritus. No systemic side-effects have been observed after absorption of the drug. In some cases, sensitization or irritation may follow its topical application, particularly to an eroded skin; however, this is more likely to be caused by the base in which it is incorporated than by prednisolone itself. The drug should not be applied to infected areas of the skin.

For topical administration, a cream containing 5 mg. of prednisolone per gram is applied to the affected areas of the skin three or four times daily.

The Council voted to amend New and Nonofficial Remedies accordingly to describe the use of prednisolone by the topical route.

Schering Corporation cooperated by furnishing scientific data to aid in the evaluation of the topical use of prednisolone.

Intramuscular Use of Crystalline Trypsin

The Council has evaluated the intramuscular use of an oil suspension of crystalline trypsin (Parenzyme) for the treatment of thrombophlebitis, phlebothrombosis, ocular inflammations, traumatic wounds, and varicose and diabetic leg ulcers. Currently available evidence suggests that many patients respond favorably to the drug. While few controlled clinical studies have been published to date, other reports indicate that a majority of patients refractory to standard modalities obtain beneficial results from trypsin administered intramuscularly. It should not be given in lieu of anticoagulants but as adjunctive therapy for reduction of inflammation and edema at the site of phlebitic processes.

Crystalline trypsin in oil produces pain and induration at the site of intramuscular injection in a sizable proportion of patients; however, the incidence of these side-effects may be appreciably reduced if a thoroughly dry and sharp needle is employed. Febrile reactions and leukocytoses, resembling those produced by parenteral administration of foreign protein, are rare. Occasionally, angioneurotic edema, hives, and urticaria occur. The drug is contraindicated or should be used with extreme caution in patients with renal or hepatic damage, blood clotting abnormalities, or hemorrhagic states. Its ultimate safety after long-term intramuscular therapy is not as yet completely determined.

Crystalline trypsin in oil is administered by deep intragluteal injection, alternating sites and buttocks. Prior to administration, sensitization tests should be performed on patients with a history of hypersensitivity. Doses of 2.5 to 5 mg., one to four times daily for three to eight days, have been administered and should be considered tentative. Dosage must be individualized and depends on the severity of symptoms and the degree of response. Adequate precautions against accidental intravenous injections should be exercised.

The Council voted to amend New and Nonofficial Remedies accordingly to describe the intramuscular use of a suspension of crystalline trypsin in oil.

The National Drug Company cooperated by furnishing scientific data to aid in the evaluation of the intramuscular use of crystalline trypsin.

MEDICINE AT WORK

CHEER UP! MORE HOSPITALS ARE SAYING SO

"If you are a maternity case you have an extremely healthy ailment. An old lady we know told her expecting granddaughters that the whole army and navy came that way."

◆

"We use 146,000 clean diapers (a year)—to dry them at the same time we would need a 90-mile clothesline (stretching from Philadelphia to New York.)"

◆

"A mechanic fixes machinery. A doctor fixes people . . . Some doctors have boys and girls of their own. Doctors love children and they work hard to make sick children well again."

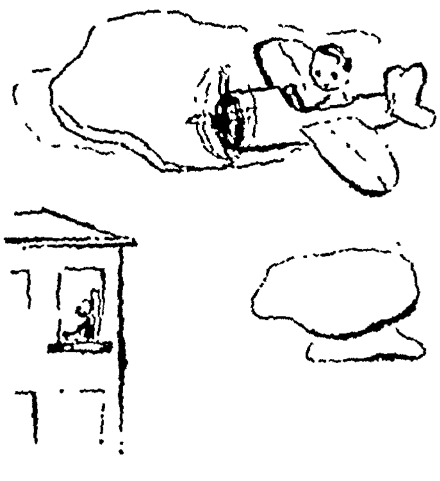
◆

"Lenox Hill is a nonprofit hospital . . . and, you will hardly believe it, in a way we are proud of losing money. It proves that we are not using a hospital bed as a milk cow."

◆

(*In answer to how many times a day a buzzer rings in the hospital*): "5,000 times. Of course 398 times are on account of old Mrs. B. . . . who wages real push-button warfare against us."

Folksy comments like these are greeting millions of hospital patients every year in sprightly booklets liberally sprinkled with cartoons, photos, and artistic use of color. The frightened child facing an operation in New York City's Memorial Center relaxes in calm curiosity of "the x-ray camera that takes a picture of the inside of your body." The depressed tubercular in Philadelphia General Hospital cannot suppress a smile at the caricature in his booklet of two patients shooting dice beside coins and bills on the ward floor—under the caption: "Gambling is not permitted in the hospital."



Adorning the cover of the Palo Alto, Calif., Hospital's patient information booklet is a sketched physician-stork standing atop a chimney on one leg and peering at a watch held in the other. Inside the pamphlet is a series of questions and answers for expectant mothers. Sample: "Q. When do I see my husband again? A. After the nurses finish preparing you for delivery, he will be called from the Heir Port."

Booklet Success Is Spreading

This sort of light informative touch has been so successful in recent years that many hospital administrators, physicians, nurses, and patients find themselves wondering why it has not been done before on a large scale. The Franklin Square Hospital in Baltimore not long ago began distributing instructional sheets for the patient (one sheet prepares him for a basal metabolism test—under the sketch of a sprawling hound and the heading: "Let's see how lazy YOU can be").

Hospital Administrator Sanford Kotzen questioned doctors who had enjoyed privileges at several hospitals—to verify that the patient information sheets were eliminating interruptions in preoperative and prediagnostic routine. One physician told Kotzen: "This is the kind of thing hospitals should have done long ago." Another said: "They should have something like these in all hospitals."

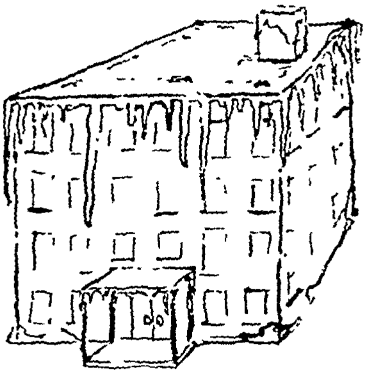
Already, the American Hospital Association notes "an increasing interest" among the nation's 7,000 hospitals in publishing informational material for the 21 million patients who go through their doors each year. At last report, 26% of the hospitals were offering this service—ranging from 11% of the proprietary general and special short-term hospitals to 50% of all tuberculosis hospitals in the United States. Now, says the A. H. A., "patients' booklets are used regularly more than any other" hospital publications, including employe information sheets, house organs, and annual reports.

Not long ago in a survey, the nearly 2,000 hospitals that publish information for patients were asked to report response to their booklets. Not one comment was unfavorable. The praises included: "Patients like it and doctors feel it helps the patient understand," and "a very valuable technique in the rapid orientation of the patient." All agreed that the price of publication was well worth the long-run public relations and immediate-cooperation value received.

Examples of effective booklets range from a two-fold sheet costing less than a penny a copy (and containing hospital rules, visitors hours, rates, cost of guest meals, and list of staff members and credentials) to a 30-page slick pamphlet with pictures and color, costing 12½ cents a copy (and carrying complete information about the hospital with line drawings on each page). Says the A. H. A.: "There is no reason why an economy-minded administration could not mimeograph essential information in a neat and readable form."

Cold Versus Warm Treatment

For years, many a doctor has been concerned with how conditions in a few "cold" hospitals have chilled tensely his otherwise warm patients at a crucial time when preoperational relaxation is so important. The physician knows that when a hospital informs his patients of the things and routine around them, and what is happening to them and why, the resulting cooperation makes for better convalescence and often a shorter stay in the hospital. At the same time, the hush-hush of the medieval medical approach is eliminated by dispelling a sometimes popular notion that medicine lies in a realm of deep dark secrets.



The 32-page illustrated handbook for patients in the new Hunterdon Medical Center in Flemington, N. J., stresses medical care as "a team problem, too complicated for any single physician to provide." That note is echoed by the University Hospital at Ann Arbor, Mich., in a booklet that lists the many hospital people who contribute to the patient's comforts.

The booklet of Boston's Peter Bent Brigham Hospital carries this reminder: "Mr. Patient sees the doctor, the nurse, the food he does not want, the early morning call, the cashier to whom he pays his bills." Then, taking the opportunity to show what today's sharply higher hospital bills are paying for, the booklet continues: "But he does not see the pharmacist, the sterile supply room, the medical record library, the instrument repair shop, the surgical supply room . . . the operating room and its costly equipment . . . the expert radiologist . . . the blood bank . . . the costly laboratory equipment and the trained personnel . . . the dietary department and the gleaming modern kitchens . . . the laundry . . . the linen and supply rooms . . . the elaborate power plant . . . the window cleaner, the refrigeration mechanic, the steam-fitter, the plumber, the carpenter, the painter, the elevator mechanic . . ."

There is greater cooperation when the patient understands what rules in the book he is expected to follow. Nurses have an easier time of it because many questions they would be asked are answered in print. All this conditioning expands the doctor-patient atmosphere of confidence and cordiality so essential to medical counseling.

Information booklets are kept in some doctors' offices so that the prospective patient can prepare for a hospital stay. This is particularly effective in maternity cases. The Presbyterian Hospital in Chicago puts out a 32-page booklet that is fine art with its gently stylized sketches of mother and child and with its easily understood advisory text covering suggested diets and also conditions before, during, and after birth. (At one point, it is stated in the booklet: "At no time are you to substitute this booklet or any other for your doctor. Nothing can take the place of the careful supervision you will receive from your physician.")

Personal Approach Does It

Most of the pamphlets are written with the personal approach. The Medical College of Virginia Hospital in Richmond asks its patients to grade the hospital in a back-page quiz on food, services, and suggestions for improvement. The University (of Michigan) Hospital tells its story in the words of a "typical" woman patient facing problems and questions encountered by any patient. Dr. Jack Weatherly, as staff psychiatrist in the Veterans Administration Hospital at Gulfport, Miss., writes that the psychiatric patient often responds favorably to the use of personal pronouns in the booklet text: "You will be seen soon by your ward doctor and, later, when your own case doctor sees you, you can spend as much time as you need to talk over your problem."

"The pen is mightier than the scalpel," says the A. H. A. in urging more hospitals to publish information for patients. The association recommends that the writing be done by people who have the same fears, confusion, and anxiety as patients—if possible, by people not in the hospital field. They say this advice has brought about the current crop of humor, lighthearted copy, and touching line drawings among the booklets being published today in the U. S. (A straightforward approach is used for psychiatric patients, since they might easily misconstrue efforts at wit and cheery pep talks.)

You can still become a patient in a hospital that is devoid of the personal touch. At some places, you can still gaze through the institutional atmosphere at things and people sterile and antiseptic—only occasionally seeing also your own physician as personification of familiar warmth and understanding. But today, as never before, you will find this picture of hospital life diminishing in the United States. Many physicians would like to see it vanish completely.

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION

Edited Under the Direction of the Board of Trustees
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Subscription price . . Fifteen dollars per annum in advance
Cable Address . . . . "Medic, Chicago"

VIRAL ETIOLOGY OF CANCER AND LEUKEMIA?

GUEST EDITORIAL

Ludwik Gross, M.D.

During the past decade the concept of viral etiology of cancer and allied diseases has gained considerable momentum. Experimental data began to accumulate pointing more and more to the possibility that many, if not all, malignant tumors may be caused by viruses. Thus, a large number of malignant tumors of different morphology and in different species of animals could be transmitted from one host to another by filtered extracts. At this time, most of the common tumors in chickens, such as the various forms of leukemia and sarcoma, have been found to be transmitted by filtered extracts. The natural epidemiology of chicken lymphomatosis through the embryonated eggs has also been established.[1] In some instances, among newly hatched chicks, the transmission may be air-borne.

The most impressive recent advances, however, in the field of viral etiology of tumors have been accomplished in mice. The fundamental discovery of Bittner[2] in 1936, showing that a certain form of breast carcinoma in the mouse is due to a virus that is transmitted in the milk from healthy (at the time of transmission) carrier mothers to their suckling offspring, could be considered the turning point in the history of modern cancer research. Fifteen years later, in 1951, mouse leukemia, a disease clinically and morphologically strikingly similar to that occurring in humans, was demonstrated[3] to be caused by a filterable virus. The use of newborn animals proved to be essential for successful transmission of the cell-free leukemic agent in mice. Shortly afterward it was found[4] that, when filtered extracts prepared from leukemic mice were inoculated into newborn animals of certain susceptible nonleukemic strains, some animals developed leukemia, whereas others developed parotid gland carcinomas and/or subcutaneous fibromyxosarcomas. These results have been recently confirmed by Woolley,[5] at the Sloan-Kettering Institute in New York. When, later, filtered extracts were prepared from parotid tumors, or sarcomas, and inoculated into newborn mice, either leukemia, or parotid tumors, and/or subcutaneous sarcomas developed. Similarly, when Graffi and co-workers[6] in Germany inoculated filtered extracts prepared from a transplanted mouse mammary carcinoma into newborn mice, a high percentage of the injected animals developed typical generalized leukemia. The question immediately arose whether one single virus may be able to induce leukemia, parotid gland tumors, subcutaneous sarcomas, or carcinomas, or whether the leukemic extracts contained a mixture of distinct, though possibly related, oncogenic agents. This question, which is of fundamental importance, has not yet been answered.

In further experiments it was demonstrated[7] that carrier mice of leukemic strains, earmarked to develop leukemia at middle age, even though in apparent good health when young, transmit the virus to their offspring. This transmission occurs not through the milk, as in the case of mammary carcinoma, but directly through the embryos, from one generation to another. Mouse leukemia, as chicken lymphomatosis, appears to be, therefore, an egg-borne virus disease. In more recent studies it has been shown that the mouse leukemia virus is a spherical particle less than 70 mμ in diameter, which can be visualized in an electron microscope,[7] and that this agent is present in various organs of the carrier animals, and in leukemic tumors and blood plasma of leukemic mice.

In all these experiments, it was necessary to inject newborn mice, only a few hours old, in order to induce, with cell-free extracts, leukemia, parotid gland tumors, or sarcomas. It appeared, therefore, that the use of an animal not more than a few hours old was essential for the successful transmission of these oncogenic agents. When, however, Friend,[8] at the Sloan-Kettering Institute in New York, inoculated cell-free extracts, prepared from a transplanted Ehrlich ascites mouse carcinoma, into newborn Swiss mice, some of the inoculated mice developed generalized leukemia 14 months later; one of these leukemias, a myelogenous form, proved to be transmissible by filtered extracts into adult Swiss mice.

There may exist, therefore, different mouse leukemia viruses, some transmissible to newborn hosts only, others to adult hosts as well. Beard[9] and his associates

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at Duke University made similar observations in their studies on chicken leukemia: whereas chicks less than 3 days old had to be used for inoculation with the myeloblastosis virus, young adult chickens could be inoculated with the virus of erythroblastosis. Although these two viruses are indistinguishable in electron micrographs, representing spherical particles about 120 m μ in diameter, they induce distinct forms of chicken leukemia.[9]

These recent developments in experimental cancer research add significantly to the older experiments in which various tumors in chickens, rabbits, frogs, and mice have been transmitted by filtered extracts. In humans thus far only warts and papillomas have been found to be transmissible by filtered extracts. By analogy, however, it is quite apparent that many other human tumors may be caused by viruses. It is entirely possible that most, if not all, malignant tumors, not only in animals but also in humans, are caused by filterable viruses. Many of these viruses may be transmitted from generation to generation,[7] remaining in a latent form harmless for their carrier hosts. Now and then, however, prompted by some obscure activating factors (some of them physiological, such as metabolic or hormonal, others extrinsic, such as chemical poisons or ionizing radiation), these hitherto dormant viruses may change into tumor-producing pathogens. Such "accidents" may happen only occasionally, separated by several generations of healthy carriers.[7]

Should this concept prove to be true, oncogenic viruses could be compared to temperate bacteriophages, transmitted from one generation to another in lysogenic bacterial hosts, only very occasionally killing some of their carriers. This concept would throw a different light on the carcinogenic action of certain chemicals as well as the development of leukemia in radiologists and in population groups exposed to ionizing radiation. It would also explain the striking, though rare, reports of familial incidence of cancer and leukemia in humans.

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE

At the Congress on Medical Education and Licensure scheduled to be held at the Palmer House, Chicago, February 10-12, 1957, the Council on Medical Education is planning its program to deal with current problems of widespread interest in medical education.

The program on Sunday morning, February 10, will be devoted to a conference on Graduate Medical Education for General Practice—1957, which will be co-sponsored by the Advisory Board for Medical Specialties and the Council. This conference will be introduced by two background statements, one presenting the role of undergraduate medical education today and the other presenting the concept of general practice regarding adequate graduate medical education in preparation for general practice—1957. These two background papers will be followed by a series of short, clean-cut presentations of what should constitute graduate medical education for general practice today as seen from the point of view of (*a*) internal medicine, (*b*) pediatrics, (*c*) surgery, (*d*) obstetrics and gynecology, and (*e*) psychiatry. Ample time will be permitted after these presentations for discussion from the floor, with the speakers acting as a panel. It is hoped that this conference will aid in better clarification of the graduate needs in preparation for general practice—1957, rather than their interpretation in the setting of some years ago. This should be an interesting and valuable conference for all concerned with internship and residency training programs in both specialty and general practice.

Sunday afternoon, February 10, will be devoted to the regular business meetings of the Advisory Board for Medical Specialties and the Federation of State Medical Boards of the United States.

Monday, February 11, will be devoted to a symposium on Medical Education Tomorrow during the morning session. The introductory paper will deal with the "lasting values in medical education" as opposed to the more transitory or temporary values. In projecting the discussion of Medical Education Tomorrow, papers will be presented on medical education as a cultural experience, the importance of and concern over natural and physical sciences remaining basic in the education of the physician, the need for structuring medical education to adequately reflect medical research in both knowledge and attitudes, and the "pros and cons" of interpretation and correlation. Efforts will be made to deal with the factors that are most important in creating the current unrest among medical educators in the search for new and better objectives, as well as techniques and methodologies.

The afternoon session on February 11 will focus attention on Postgraduate Medical Education. The keynote of this session will deal with the importance and challenges presented by this field. This will be followed by a presentation of the development of medical school-state medical society postgraduate programs (an analysis of the Kansas story). The role of a community hospital in continuing education will be highlighted by the Hunterdoon experiment and the potential significance of its general pattern to postgraduate medical education. The regional-hospital-medical school affiliation potentialities as exemplified by such programs as the Michigan Plan and the New York University Plan will also be presented. This program should also be of high interest to hospital administrators, state and local medical societies, and directors of postgraduate programs of medical education as well as to medical school administrators and faculty personnel.

The Federation of State Medical Boards of the United States will hold their Annual Federation Banquet on Monday evening, February 11. On Tuesday, February 12, the Federation will conduct its annual program around the general theme of "Re-evaluation of the Licensing Examination." This challenging area of concern should be of interest to those engaged in the various aspects of undergraduate and graduate medical education as well as to those concerned with licensure.

MEDICAL NEWS

CALIFORNIA

Society News.—The Los Angeles Physicians' Art Society has elected Dr. Douglas D. McKinnon, president; Dr. Alonzo B. Cass, president-elect; and Dr. Victor M. Marshall, secretary-treasurer. Dr. Samuel P. Danno, this year's winner, received the society's rotating "Oscar" from Dr. William M. Nethery, Glendale.

Physicist to Address Cardiac Conference.—The Cardiac Surgical Conference at Mount Zion Hospital, San Francisco, will be addressed by Norbert Wiener, Ph.D., who will speak at 10:15 a. m. Dec. 1 in Herbst Hall on "Use of the Ballistocardiogram as Evidence of Vascular Dynamics." Dr. Wiener is professor of physics at Massachusetts Institute of Technology in Cambridge.

Personal.—Dr. John R. Upton, assistant clinical professor of obstetrics and gynecology, University of California Medical School, Berkeley-San Francisco, has been appointed by Queen Elizabeth II as an associate officer in the Order of St. John for "his pioneer work in blood banking and his service to the British Commonwealth of Nations." This order of chivalry, which is over 900 years old, discarded its military status in 1888 and became a purely service organization.

CONNECTICUT

Course on Economics of Medical Practice.—The Connecticut State Medical Society, in cooperation with Yale University School of Medicine, New Haven, department of public health, is sponsoring a course on the economics and relationships of medical practice at the Brady Auditorium, 310 Cedar St., New Haven. At 8 p. m., Dec. 5, a special lecture, "Role of the Physician in Preventive Medicine," will be delivered by Dr. Dwight H. Murray, Napa, Calif., President, American Medical Association. On Dec. 13, the series on "Careers in Medicine" will be continued with a discussion on surgery by Drs. Edward J. Ottenheimer, Willimantic, and William H. Curley Jr., Bridgeport.

FLORIDA

Medical Society Honors First Graduating Class.—At a pregraduation dinner sponsored by the faculty of the first graduating class of the University of Miami School of Medicine, Coral Gables, the Dade County Medical Association presented an engraved plaque bearing the English translation of the oath of Hippocrates. A brass plate below the engraving is inscribed: "Presented to the University of Miami School of Medicine in honor of its first graduating class June 11, 1956 by the Dade County Medical Association. Hunter B. Rogers, President, Vincent P. Corso, Secretary." Dr. Rogers was invited by Homer F. Marsh, Ph.D., professor of bacteriology and dean of the medical school, to administer the oath to the new physicians.

ILLINOIS

Lecture in Winnetka.—Dr. Lauretta Bender, professor of clinical psychiatry, New York University College of Medicine, and principal research scientist in child psychiatry, New York State Department of Mental Hygiene, will present "Problems of Early Development" Dec. 5, 8 p. m., at the North Shore Health Resort, 225 Sheridan Rd., Winnetka. Physicians are invited.

Meeting on Physical Medicine.—The Chicago Society of Physical Medicine and Rehabilitation will hold its regular meeting Dec. 1, 2 p. m., at the Institute of Physical Medicine and Rehabilitation, 619 N. Glen Oak Ave., Peoria. The program, "The Physiatrist and the Patient's Physician," will be presented by the medical staff, Institute of Physical Medicine and Rehabilitation, and representative members of the medical staffs of St. Francis Hospital and the Methodist Hospital of Central Illinois. At 3 p. m. there will be a tour of the institute. A social hour, 5 p. m., will precede dinner.

Chicago

Lectures on History of Surgery.—The International College of Surgeons is sponsoring a series of lectures on the history of surgery at the Surgeons' Hall of Fame, 1524 Lake Shore Dr. All physicians will be welcome to attend. On Dec. 4, "The Middle Ages in Medicine and the School of Salerno" will be considered by Mr. Loren MacKenney, professor of history, University of North Carolina, Chapel Hill.

Society News.—The Institute of Medicine of Chicago will hold its 41st annual meeting Dec. 4 at the Furniture Club of America, 17th floor, 667 N. McClurg Ct. (telephone during the meeting: WHitehall 4-8552). The open meeting at 8 p. m. will be preceded by the annual reception, 6 p. m., and dinner, 7 p. m., for fellows of the institute, their wives, and other guests. The presidential address, "The Medical Outlook from Washington, D. C." will be delivered at 9 p. m. by Dr. Lowell T. Coggeshall.

Symposium on Parenteral Therapy with Fluids.—A symposium on parenteral therapy with fluids, co-sponsored by the Chicago Medical Society and Baxter Laboratories, Inc., will be held at the Sheraton Hotel, Dec. 5-6, in connection with the 25th anniversary of Baxter Laboratories and pioneering by Chicago physicians in the development of such therapy. All physicians are invited to attend. There is no registration fee. The program, which will open with a review of the development of parenteral therapy with fluids by Dr. Karl A. Meyer, president, Chicago Medical Society, will include the following presentations:

Physiology of Acid Base Balance, Harry F. Weisberg, Chicago.
Diagnosis of Fluid Electrolyte Imbalance, Harvey R. Bernard, St. Louis
Third Body Space—Translocation of Fluid, Parker Vanamee, New York City.
Special Pediatric Problems, Charles U. Lowe, Buffalo.
Therapy of Fluid Electrolyte Problems, Carl O. Rice, Minneapolis.
Use of Blood, Ralph M. Hartwell, New Orleans.
Use of Plasma Volume Expanders, Jacob J. Weinstein, Washington, D C
Treatment of Burns, Major Bruce G. MacMillan, M.C., Brooke Army Medical Center, Fort Sam Houston, Texas.
Carbohydrates, Rachmiel Levine, Chicago.
Vitamins, Tom D. Spies, Birmingham.
Protein, William E. Abbott, Cleveland.
Fat, Frederick J. Stare, Boston.

IOWA

Tumor Conference.—The Iowa division, American Cancer Society, and the University Hospitals, State University of Iowa College of Medicine, Iowa City, will present a tumor conference Dec. 7-8. A symposium on leukemias and lymphomas will be conducted at 11 a. m. Friday, by Drs. Willis M. Fowler, John R. Carter, and Higdon B. Elkins. "Viruses and Cancer" by Dr. Richard E. Shope, Rockefeller Hospital for Medical Research, New York City, will be presented at 4:10 p. m. Friday, and a lecture on bone cancer, with special reference to cartilaginous tumors, will be given at 11 a. m. Saturday, by Dr. Granville A. Bennett, professor of pathology, University of Illinois College of Medicine, Chicago. The program will also include the following presentations by Iowa City participants:

Gynecologic Cancer—Helpful Hints in Diagnosis, William C. Keettel.
What Therapy Can Do for Female Pelvic Cancer, John H. Randall.
Cancer of the Breast. A Quarter Century at University Hospitals, Robert C. Hickey.
Palliation of Advanced Breast Cancer, Robert T. Tidrick.
The Pediatrician Discovers a Mass—What Then? John D. MacQueen.
The Surgeon and the Child with Cancer, John A. Gius.
Urological Diagnostic Hints, Raymond G. Bunge.
Recent Changes in Therapy of Cancer of the Gastrointestinal Tract, Rubin Flocks.
The Place of Isotopes in Cancer Care: Present and Future Potentials, Titus Evans, Ph.D.
Lesions Produced by Aminonitriles, Ignacio V. Ponseti.
Dermatologist and Cutaneous Cancers, Ruben Nomland.
Special Problems in Cutaneous Cancer for the Surgeon, Sidney E. Ziffren
Shadow in the Lung—the Internist, Paul M. Seebohm.
Shadow in the Lung—the Surgeon, Johann L. Ehrenhaft.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

Dr. Marc Hollender Goes to Syracuse.—Dr. Marc H. Hollender, associate professor of psychiatry, University of Illinois College of Medicine, and staff member of the Institute for Psychoanalysis, has been appointed professor and chairman of the department of psychiatry at State University of New York College of Medicine at Syracuse. Dr. Hollender succeeds Dr. Edward J. Stainbrook, who resigned last February to become professor and chairman of psychiatry at the University of Southern California, Los Angeles, and chief of psychiatric services at Los Angeles County Hospital. Dr. Hollender has been affiliated with Cook County Hospital and the University of Illinois Neuropsychiatric Institute. From 1942 to 1946 he served in the Air Force Medical Corps. In 1949 he received certification in psychiatry from the American Board of Psychiatry and Neurology.

MASSACHUSETTS

Dr. Hume Goes to Virginia.—Dr. David M. Hume, assistant professor of surgery and director of surgical research at the Harvard Medical School, Boston, has been appointed professor of surgery at the Medical College of Virginia, Richmond, to succeed the late Dr. Isaac A. Bigger. He assumed his duties as professor and head of the department of surgery on Aug. 16.

Dr. Lennox Honored.—Dr. William G. Lennox, associate professor emeritus in neurology at Harvard Medical School, Boston, has been chosen by the American Pharmaceutical Manufacturers' Association as the recipient of its scientific award for his research on the adaption of psychotherapeutic agents in the treatment of mental diseases. Dr. Lennox is a past-president of the International League Against Epilepsy and a founder of the American Epilepsy League. The presentation to Dr. Lennox will be made at the mid-year meeting of the association, Dec. 11 at the Waldorf-Astoria Hotel in New York City.

Dr. Solomon Becomes Emeritus Professor.—Dr. Harry C. Solomon, Boston, who helped to shape the early development of the teaching of psychiatry in the Harvard Medical School, has become emeritus professor of psychiatry, but will continue as medical director and superintendent of the Boston Psychopathic Hospital, the major center for the teaching of psychiatry in the medical school. He is currently president-elect of the American Psychiatric Association and president of the Association for Research in Nervous and Mental Disease. Dr. Solomon served as a first lieutenant with the Army Medical Corps in 1918-1919 and during World War II was chief neuropsychiatric examiner of the Boston Recruiting and Induction Station and a consultant to the Secretary of War. Among his many scientific publications are "Syphilis of the Innocent," "Studies in Lobotomy," "Neurosyphilis," "The Frontal Lobes and Schizophrenia," and "Manual of Neuropsychiatry," of which he was co-editor.

MICHIGAN

Symposium on Trauma.—The fifth annual Symposium on Trauma, sponsored by the Wayne State University Medical School, Detroit, and the Michigan Regional Committee on Trauma, will be held Dec. 5. Exhibits will be shown in the morning at the Farwell Building. A complimentary luncheon sponsored by the Upjohn Company will be given in the Medical School Cafeteria. The presentation of Dr. Henry C. Marble, Boston, the afternoon guest speaker, will be followed by two panel discussions in the auditorium of the Lafayette Clinic Registration fee is $2. Interns and residents will be admitted free.

NEW JERSEY

Doctors' Chorus Aids Chronically Ill.—The doctors' chorus of the Essex County Medical Society recently presented to the Essex County service for the chronically ill $1,300, the net proceeds of the 1956 benefit concert, bringing to $11,500 its contributions to this service. The chorus closed its 1955-1956 season with the third benefit concert for the Roseville Y.M.C.A.

Visiting Chiefs at Hospital.—The Atlantic City Hospital will have as visiting chiefs pro-tem Dr. Bernard Fisher, assistant professor of surgery, University of Pittsburgh School of Medicine, Dec. 3-7; Dr. William T. Fitts Jr., associate professor of surgery, University of Pennsylvania School of Medicine, Philadelphia, Dec. 10-14; Dr. S. Leon Israel, associate professor of obstetrics and gynecology, University of Pennsylvania Graduate School of Medicine, Philadelphia, Dec. 17-19; Dr. Charles W. Charny, associate in urology, Hahnemann Medical College and Hospital of Philadelphia, Dec. 20-21.

Tumor Seminar.—The sixth annual slide seminar on "Unusual Tumors," sponsored by the New Jersey Society of Clinical Pathologists and the New Jersey State Department of Health, bureau of pathology, will be held at 2 p. m., Dec. 8, in the Essex House, Clinton and Broad streets, Newark. The moderator will be Dr. Arthur P. Stout, Institute for Cancer Research, Columbia University College of Physicians and Surgeons. All physicians are welcome. A social hour and dinner, with Dr. Stout as guest, will be held at the Essex House after the seminar. Reservations for the dinner may be made through Dr. Murray W. Shulman, Irvington General Hospital, Irvington, chairman of the seminar.

Annual Martland Lecture.—The Essex County Pathological and Anatomical Society will present the 20th annual Harrison S. Martland Lecture, Dec. 5, at the Academy of Medicine, 91 Lincoln Pk., Newark. Dr. Sidney Farber, professor of pathology, Harvard Medical School, and director of the Cancer Research Foundation at the Children's Hospital Center, Boston, will discuss "Progress in the Treatment and Control of Cancer." The meeting, which will be held in conjunction with the Academy of Medicine of New Jersey and the Essex County Medical Society, will be preceded by dinner at the Essex House Hotel, Broad Street. Reservations, $5 per person, should be sent to Dr. Murray W. Shulman, 913 20th St., Newark 8. All members of the profession are invited.

NEW MEXICO

Society News.—The New Mexico Medical Society has appointed Dr. Aaron E. Margulis, Santa Fe, as its state scientific editor and member of the *Rocky Mountain Medical Journal* editorial board, to succeed Dr. Carl H. Gellenthien, Valmora, who retired from the editorship after almost 12 years of service.

NEW YORK

Lecture in Gerontology.—Dr. Edmund V. Cowdry, director of the division of cancer research, Washington University School of Medicine, St. Louis, will deliver the third annual Lecture in Gerontology at the Hospital Division, Brooklyn Hebrew Home & Hospital for the Aged, 813 Howard Ave., Brooklyn, Dec 6, 8:30 p. m.

Assembly on Anesthesiology.—The 10th Postgraduate Assembly of the New York State Society of [illegible]tel New Yorker, New York City, Dec. [illegible]; at 9:30 a. m. with simultaneous panels on "Blood Transfusions: Problems, Results, Medicolegal Responsibilities" and "Current Trends in the Study of Kidney Function." Out-of-state participants in the former panel include C. Joseph Stetler, LL.M., director, Law Department, American Medical Association, Chicago, and Dr. William G. Workman, Bethesda, Md.; in the latter, Drs. Frederic C. Bartter, Bethesda, Md., and Joseph E. Murray, Boston. After roundtable luncheons at 12:30 p. m., panels will be presented on "Light Anesthesia, Balanced Anesthesia, or Polypharmacy" and "Circulatory Stress." Out-of-state participants in the former will include Drs. C. Ronald Stephen, Durham, N. C., and Philip D. Woodbridge, Greenfield, Mass., and in the latter, Dr. Howard A. Frank, Boston. On Thursday afternoon, there will be a closed circuit telecast. The New York State Society of Anesthesiologists will be hosts at the annual cocktail party (7 p. m.) and dinner-dance (8 p. m.), honoring Dr. Emory A. Rovenstine, New York City. Friday morning Dr. Robert M. Smith, Boston, will serve as chairman on a panel, "Management of the Infant for Surgery," in which the participants will be Drs. C. Everett Koop, Philadelphia; William O. McQuiston, Peoria, Ill.; and Earle L. Wrenn Jr., Memphis, Tenn. Simultaneously, Dr. James E. Eckenhoff, Philadelphia, will be chairman of a panel on antidotes in anesthesiology, with the following collaborators: Dr. John Adriani, New Orleans,

Mathae, George Herman ⊕ St. Louis; St. Louis University School of Medicine, St. Louis, 1909; also a dentist and lawyer; on the staff of the Bethesda General Hospital and the Lutheran Hospital, where he died Sept. 22, aged 74, of cerebral arteriosclerosis.

McGee, James Patton ⊕ Oklahoma City; Emory University School of Medicine, Atlanta, Ga., 1916; professor of ophthalmology at the University of Oklahoma School of Medicine; died in St. Anthony Hospital Sept. 11, aged 65, of myocardial infarction.

McHugh, Francis Thomas ⊕ Chippewa Falls, Wis.; Bennett Medical College, Chicago, 1911; interned at the Cook County Hospital in Chicago; died Sept. 5, aged 75, of coronary thrombosis.

McLeod, Frederick Leon, Los Angeles; Lincoln Medical College of Cotner University, Lincoln, Neb., 1901; College of Physicians and Surgeons, Baltimore, 1907; an associate member of the American Medical Association; formerly practiced in Lincoln, Neb., where he was on the staff of St. Elizabeth Hospital; died Aug. 24, aged 77, of subarachnoid hemorrhage and congestive heart disease.

Meredith, Loren Kenneth ⊕ Des Moines, Iowa; University of Michigan Medical School, Ann Arbor, 1916; member of the American Academy of General Practice and the Association of Life Insurance Medical Directors of America; veteran of World War I; medical director for the National Life Company and the Iowa Life Insurance Company; died in the Rochester Methodist Hospital, Rochester, Minn., Sept. 13, aged 65, of an abdominal hemorrhage.

Miller, George William ⊕ Norristown, Pa.; Jefferson Medical College of Philadelphia, 1906; fellow of the American College of Surgeons; served as professor of general anatomy in the Temple University School of Dentistry, Philadelphia, as associate in anatomy at his alma mater, and on the staff of the department of applied anatomy at Temple University School of Medicine in Philadelphia; veteran of World War I; on the staffs of the Sacred Heart Hospital and the Montgomery Hospital, where he died Sept. 5, aged 74, of chronic lymphatic leukemia.

Moore, Leland Oliver Walter ⊕ Colonel, U. S. Army, retired, Washington, D. C.; Cooper Medical College, San Francisco, 1912; veteran of World War I; entered the Medical Corps of the U. S. Army in 1920 and retired Nov. 30, 1945; fellow of the American College of Surgeons; formerly professor of military science and tactics at George Washington University School of Medicine; died in the Walter Reed Army Hospital Aug. 28, aged 67, of cancer.

Murphy, Jewyl Booth, Redwood City, Calif.; University of Texas School of Medicine, Galveston, 1922; member of the American Academy of Pediatrics; interned at the Children's Hospital in San Francisco, where she was on the staff of the University of California Hospital; formerly on the staff of the Community Hospital of San Mateo County in San Mateo; died Aug. 30, aged 60, of carcinoma of the colon.

Nelson, Oscar Emil, Stewart, Minn.; Chicago College of Medicine and Surgery, Chicago, 1910, died Aug. 19, aged 79, of cancer.

Nicoll, Alexander, New York City; Columbia University College of Physicians and Surgeons, New York City, 1903, an associate member of the American Medical Association; fellow of the American College of Surgeons; veteran of World War I; at one time on the faculty of Fordham University School of Medicine; served on the staffs of the Central Suffolk Hospital in Riverhead, St. Elizabeth's, Fordham, Mother Cabrini Memorial and St. Francis' hospitals; died in the Southside Hospital, Bay Shore, Sept. 24, aged 75.

Nilson, Helmer Jonas ⊕ North Mankato, Minn.; University of Minnesota Medical School, Minneapolis, 1932; member of the American Academy of General Practice; served as health officer; on the staffs of St. Joseph's Hospital and the Immanuel Hospital, Mankato, where he died Aug. 31, aged 63, of a coronary attack.

North, William R. ⊕ Nokomis, Fla.; Beaumont Hospital Medical College, St. Louis, 1900; member of the Missouri State Medical Association; formerly practiced in St. Louis, where he was on the staff of the Evangelical Deaconess Hospital; died in Labadie, Mo., Aug. 29, aged 80, of cancer.

Ogden, Arthur White ⊕ Joliet, Ill.; the Hahnemann Medical College and Hospital, Chicago, 1913; died Aug. 17, aged 72, of arteriosclerotic heart disease.

Ogden, Michael Alexander ⊕ Passaic, N. J.; University of Odessa Faculty of Medicine, Odessa, Russia, 1918; specialist certified by the American Board of Pathology; fellow of the American College of Physicians; served on the faculty of the Louisiana State University School of Medicine in New Orleans; for many years on the staff of the Passaic General Hospital, where he died Sept. 13, aged 63, of coronary disease.

Oliver, Adlai Stevenson ⊕ Raleigh, N. C.; Jefferson Medical College of Philadelphia, 1914; specialist certified by the American Board of Obstetrics and Gynecology; on the staffs of the Rex and St. Agnes hospitals; died Aug. 20, aged 64, of coronary artery disease.

Orr, James Edward, Seneca, S. C.; Medical College of South Carolina, Charleston, 1931; died Aug. 28, aged 53, of coronary thrombosis.

Outland, James Alfred, Murray, Ky.; University of Louisville School of Medicine, Louisville, 1912; member of the Kentucky State Medical Association; public health physician for Graves, Calloway, and Trigg counties; died Aug. 24, aged 71, of cancer.

Mackenzie, Simon Samuel ⊕ Akron, Ohio; University of Buffalo School of Medicine, Buffalo, 1897; for many years practiced in Warren, where he was on the staff of the Warren Memorial Hospital; died Aug. 24, aged 83, of heart disease.

Pace, Arthur Albert ⊕ Toledo, Iowa; Detroit College of Medicine, Detroit, 1896; veteran of World War I; served as mayor, councilman, and member of the school board; formerly associated with the Indian Service; on the staff of the Evangelical Hospital, Marshalltown; died Aug. 8, aged 86, of heart disease.

Palmer, Mary Simpson McCarty, Orchard Lake, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1886; died Sept. 11, aged 94, of heart disease.

Pedrick, William Weaver ⊕ Glassboro, N. J., Temple University School of Medicine, Philadelphia, 1922; member of the Industrial Medical Association; for many years president of the Gloucester County Health Association, and physician for the public schools; past-president of the board of health; died in the Elmer (N. J.) Community Hospital Aug. 10, aged 60, of coronary thrombosis.

Philo, Rae Morris, New Haven, N. Y.; Syracuse University College of Medicine, Syracuse, 1913; died July 28, aged 67, of angina pectoris.

Price, John Thomas, Harrodsburg, Ky.; Hospital College of Medicine, Louisville, 1895; an associate member of the American Medical Association; died in the James B. Haggin Memorial Hospital Aug. 14, aged 88.

Price, Lucius Grant, St. Petersburg, Fla.; University of Pennsylvania Department of Medicine, Philadelphia, 1890; died Aug. 12, aged 89, of arteriosclerosis.

Quinn, Francis Peter ⊕ Dubuque, Iowa; State University of Iowa College of Medicine, Iowa City, 1921; member of the American Academy of Ophthalmology and Otolaryngology; served during World War II; died Aug. 8, aged 64, of bronchial asthma.

Rauchschwalbe, Lothar Ernst ⊕ Oconto Falls, Wis.; Loyola University School of Medicine, Chicago, 1930; on the staff of the Community Memorial Hospital, died Aug. 12, aged 53, of coronary occlusion.

Rebbeck, Elmer William, Pittsburgh; Hahnemann Medical College and Hospital of Philadelphia, 1925; an associate member of the American Medical Association, fellow of the American College of Surgeons; veteran of World War II; on the staff of the Shadyside Hospital, where he died Aug. 19, aged 54, of arteriosclerotic heart disease and pulmonary embolism.

Rice, Edward Martin ⊕ Wauwatosa, Wis., Milwaukee Medical College, Milwaukee, 1903, also a graduate in law; honorary member of the staff, St. Luke's Hospital in Milwaukee; died Aug. 26, aged 83, of uremia.

Roberts, Edward Russell ⊕ Bridgeport, Conn.; Medical School of Maine, Portland, 1913, specialist certified by the American Board of Otolaryngology; member of the American Laryngological, Rhinological and Otological Society; fellow of the American College of Surgeons; veteran of World War I; past-president of the Bridgeport Medical Society; on the staff of the Bridgeport Hospital; died Aug. 26, aged 67, of cerebral hemorrhage.

Robertson, William S., Danville, Va.; College of Physicians and Surgeons, Baltimore, 1885; died in Lynchburg Aug. 23, aged 95, of cerebral vascular accident and arteriosclerosis.

Rogers, Edmund Augustus ⊕ Brookline, Mass.; Baltimore Medical College, Baltimore, 1904; veteran of World War I; died in the New England Deaconess Hospital, Boston, Aug. 31, aged 74, of acute myocardial infarction.

Schwarzmann, Markus ⊕ New York City; Julius-Maximilians-Universität Medizinische Fakultät, Würzburg, Bavaria, Germany, 1922; died Sept. 6, aged 63, of cancer of the rectum.

Spearman, Clyde Herman, Coffeeville, Miss.; University of Nashville Medical Department, Nashville, Tenn., 1906; died Sept. 17, aged 72, in an automobile accident.

Spencer, Floyd Henry ⊕ St. Joseph, Mo.; Central Medical College of St. Joseph, 1900; veteran of World War I; past-president of the Buchanan County Medical Society; past-president of the city board of health; member and past-president of the staff, Missouri Methodist Hospital; member of the staff of St. Joseph's Hospital; past-president of the staff of State Hospital No. 2; died in the Veterans Administration Hospital, Wadsworth, Kan., Oct. 4, aged 77, of cardiac hypertrophy.

Stapp, Fred Brown ⊕ Chattanooga, Tenn.; Bellevue Hospital Medical College, New York City, 1884; past-president of the Hamilton County Medical Society; for many years medical examiner for Metropolitan Life Insurance Company; served as chief of staff at Baroness Erlanger Hospital; died Aug. 4, aged 95.

Stattman, Bernard ⊕ Brooklyn, N. Y.; University and Bellevue Hospital Medical College, New York City, 1908; on the staff of the Samaritan Hospital, where he died Aug. 27, aged 69, of coronary thrombosis.

Steele, Ernest Richmond, Dover, Del.; Jefferson Medical College of Philadelphia, 1901; died in the Kent General Hospital June 29, aged 80, of myocardial infarction.

Stewart, Thomas Weir ⊕ Lithonia, Ga., University of Louisville Medical Department, Louisville, Ky., 1915; died Aug. 13, aged 69, of pulmonary edema and coronary occlusion.

Swanson, Albert John, Costa Mesa, Calif., Chicago College of Medicine and Surgery, Chicago, 1908, an associate member of the American Medical Association, died July 10, aged 74, of cancer.

Swetlow, George Irving ⊕ Brooklyn, N. Y.; Long Island College Hospital, Brooklyn, N. Y., 1920; also a lawyer; served on the faculty of the Brooklyn Law School; fellow of the American College of Physicians; consulting neuropsychiatrist at Cumberland Hospital; died in the Brooklyn Hospital Aug. 20, aged 58, of pulmonary edema, coronary heart disease, and diabetes mellitus.

Taylor, Willis Harvey, Omaha; University of Nebraska College of Medicine, Omaha, 1911; professor emeritus of clinical obstetrics and gynecology at his alma mater; an associate member of the American Medical Association; member of the Central Association of Obstetricians and Gynecologists; fellow of the American College of Surgeons, in 1941 elected president of the Nebraska Methodist Hospital; on the staff of the Immanuel Hospital; died Aug. 5, aged 69, of coronary thrombosis.

Thomson, Joseph Oscar, Stillwater, Okla.; McGill University Faculty of Medicine, Montreal, Canada, 1909; for many years a missionary in China; fellow of the American College of Surgeons; formerly physician at the Oberlin College in Oberlin, Ohio; served as medical director for the General Motors Tank Plant in Flint, Mich.; retired in 1951 from the faculty of the Oklahoma Agricultural and Mechanical College; died in the Stillwater Municipal Hospital Oct. 2, aged 71, of cerebral hemorrhage.

Tompkins, Rutledge Chaney, Minden, La.; University of Nashville Medical Department, Nashville, Tenn., 1901; for many years coroner of Webster Parish, and associated with the Webster Parish Health Unit in Minden and Springhill; at one time medical superintendent of the State Colony and Training School in Alexandria; died July 21, aged 79, of coronary thrombosis.

Totman, Harold Maydole ⊕ Syracuse, N. Y.; Syracuse University College of Medicine, Syracuse, 1924; veteran of World War I; served on the staff of St. Joseph's Hospital; medical director of the Unity Life and Accident Insurance Company; died in St. Joseph's Hospital Aug. 5, aged 59, of lung cancer.

Townsend, Jesse P., Berryman, Mo., Beaumont Hospital Medical College, St. Louis, 1897; died in the Farmington (Mo.) State Hospital Sept. 2, aged 83.

Trippel, Edward ⊕ O'Fallon, Ill., St. Louis University School of Medicine, St. Louis, 1912; died in St. Elizabeth's Hospital, Belleville, Aug. 22, aged 67, of diabetes mellitus.

Voorhees, Bert Grant, Elmira, N. Y., Jefferson Medical College of Philadelphia, 1914; an associate member of the American Medical Association; served in France during World War I; on the staffs of Arnot-Ogden Memorial and St. Joseph's hospitals; died Sept. 29, aged 70, of cerebral hemorrhage

Waddell, William Everett, Los Angeles; Pulte Medical College, Homeopathic, Cincinnati, 1887; specialist certified by the American Board of Otolaryngology; an associate member of the American Medical Association; fellow of the American College of Surgeons; served on the staff of St. Vincent's Hospital, where he died Aug. 24, aged 91, of pulmonary thrombosis.

Walch, John Joseph ⊕ Escanaba, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1912; past-president of the Upper Peninsula Medical Society; served as a member of the state board of registration in medicine. past-president of the Delta County Medical Society; formerly a member of the board of education; a member of the board of directors of the State Bank of Escanaba; on the staff of St. Francis Hospital, where he died Sept. 5, aged 69, of cerebral thrombosis.

Weisbrod, Samuel Lyon, Milford, Mich.; Trinity Medical College, Toronto, Ontario, Canada, 1894; died Aug. 21, aged 87, of coronary thrombosis.

Wheelock, Harry Elmer ⊕ Fredonia, N. Y.; Jefferson Medical College of Philadelphia, 1914; fellow of the American College of Surgeons; veteran of World War I; for many years a member and president of the school board; a member of the board of visitors of Fredonia State Teachers College, and of the Roswell Park Memorial Institute in Buffalo; on the staff of the Brooks Memorial Hospital in Dunkirk, where he died Aug. 25, aged 65, of coronary thrombosis.

Whitehead, John Maloy ⊕ Indianapolis; Indiana University School of Medicine, Indianapolis, 1918; veteran of World War I; retired chief anesthetist for Methodist Hospital, where he died Aug. 9, aged 67, of cerebral infarction.

Wiese, Milton Arthur ⊕ Libertyville, Ill.; University of Illinois College of Medicine, Chicago, 1914; on the staffs of St. Therese Hospital in Waukegan and the Condell Memorial Hospital in Libertyville, where he died Sept. 18, aged 64, of coronary occlusion.

Willey, Arthur J., Marion, Ohio; Ohio Medical University, Columbus, 1898; fellow of the American College of Surgeons; also a dentist; on the staff of the Marion General Hospital; died Sept. 1, aged 84, of cerebral hemorrhage.

Williams, Frederick Russell ⊕ Worcester, Mass.; Long Island College Hospital, Brooklyn, N. Y., 1905; died in the Memorial Hospital Aug. 10, aged 73.

Williamson, Walter Scott ⊕ Captain, U. S. Army, San Antonio, Texas; University of Oklahoma School of Medicine, Oklahoma City, 1950; interned at the Mercy Hospital and at the University Hospitals in Oklahoma City, Okla.; resident at the Brooke Army Hospital; died in Fort Sam Houston July 8, aged 34, of coronary thrombosis.

Winters, William Winfred, Boliver, Tenn.; University of Nashville Medical Department, 1904; veteran of World War I; formerly on the staff of the Western State Hospital in Western State Hospital; at one time on the staff of the Veterans Administration Hospital in Minneapolis; served as resident physician at the Davidson County Hospital in Nashville; died Aug. 14, aged 80, of bronchopneumonia and adenocarcinoma of the prostate.

Williams, Philip Banatyne, Rome, Pa.; Jefferson Medical College of Philadelphia, 1895; died in the Robert Packer Hospital, Sayre, Aug. 11, aged 82, of arteriosclerotic heart disease.

FOREIGN LETTERS

AUSTRIA

Tuberculous Appendicitis.—At the meeting of the Society for Pediatrics in Vienna on May 9, Dr. H. H. Orel presented the case of a 14-year-old boy who had received orthopedic treatment since his 4th year because of the sequels of tuberculous coxitis. In February, 1956, a tuberculous inflammation of the knee joint had developed after a fall. In the middle of March, the patient had an acute attack of appendicitis and his appendix was removed. Several days after the operation, symptoms of a tuberculous meningitis appeared, and clinical and bacteriological studies corroborated this diagnosis. The meningitis subsided after treatment with streptomycin. Histological examination of the removed appendix revealed tuberculosis of the appendix. The concurrence of the tuberculous appendicitis, meningitis, and arthritis is regarded as the result of a hematogenous dissemination of the tuberculosis resulting from the fall. Dr. Orel stated that the appendicitis was an isolated process.

Personality of Obese Children.—At the same meeting Dr. H. E. Huber reported personality studies of 50 obese children and 50 children of normal weight. The obese children came from families that were not unusual except that there seemed to be a familial tendency to obesity; most of the children ate more than the average child, and their play and games usually involved little exercise. Intelligence tests revealed that the obese children had normal intelligence, memory, perseverance, dexterity, and fantasy and average school performances, but they were relatively inactive, slow or lazy, and defective in social contacts. This last factor was not primary but was the result of the reactions of others to their physical abnormality and their inactivity.

SWITZERLAND

Aldosterone Hypersecretion in Pituitary Basophilism and Adrenal Cortical Hyperfunction.—For many years it was supposed that a hypersecretion of mineralocorticoids might play a role in the pathogenesis of those cases of pituitary basophilism and adrenal cortical hyperfunction that were associated with edema, polyuria, hypernatremia, alkalosis, and hypokalemia, but no conclusion could be reached until a method of assaying the urinary excretion of aldosterone became available. J. P. Doret (*Semaine hôp. Paris* 32:2921, 1956) found the mineralocorticoid level to be either normal or increased in patients with this condition but could not explain these contradictory findings. In the three patients with this condition reported, the presence of a marked retention of water and sodium and of alkalosis with hypokalemia suggested hyperaldosteronism. In the first case, which occurred subsequent to a large chromophobe tumor, no hormone evaluation was available; in the second (reported by Brown and co-workers), there was an increase in excretion of aldosterone; and in the third (the author's second case), due to the presence of a mixed adenocarcinoma of the pituitary gland, hyperaldosteronuria could be demonstrated.

Streptococcus Typing.—A. Rivkine (*Schweiz. med. Wchnschr.* 86:1098, 1956) reports an attempt to type the hemolytic streptococci in children of a more or less homogeneous environment (from orphanages and boarding schools). He found that, since virulence is a potential and labile characteristic, independent of the strain of the pathogen, it is not possible to predict whether a carrier will be dangerous. No laboratory test reveals the virulence for man of a given strain. A strain from a sick carrier is more likely to be virulent than one from a healthy carrier. The occurrence of a disease in the carrier of a virulent strain depends on the susceptibility or resistance of the carrier. The communicability of a strain does not seem to be correlated with its virulence. If patients are to be isolated, those with the same type should be grouped together. Even when this precaution is taken, there is the risk of reimplantation of the common strain at an increased level of virulence.

UNITED KINGDOM

Hepatic Coma.—Dr. Sheila Sherlock and co-workers (*Lancet* 2:689, 1956) showed that clinical findings similar to those in spontaneously developing hepatic coma can be induced in patients with liver disease by the oral administration either of a high-protein diet or of nitrogenous compounds, such as urea or methionine. They believe that, by passing through a diseased liver, nitrogenous materials in the intestine reach the systemic circulation and thus the brain. This theory suggested the treatment of impending hepatic coma by withdrawal of protein and nitrogen-containing substances. The authors reported a series of 66 patients with liver disease complicated by hepatic coma or precoma whom they treated in this way. As the bacterial flora of the small intestine are increased in hepatic cirrhosis, chlortetracycline was administered to reduce their number and their effect on methionine. The patients suffered from such conditions as acute viral hepatitis, hepatic cirrhosis, obstructive jaundice, and ischemic necrosis of the liver. Three lines of treatment were used: 1. The intestines were emptied and kept free of all nitrogen-containing substances. 2. All dietary protein was stopped. 3. About 1,600 calories were supplied daily as glucose drinks or as 20% glucose given through an intragastric drip or, if necessary, as dextrose given intravenously. During the recovery period, protein was added in 20-gm. increments on alternate days. Any relapse was treated by withdrawing all protein. The lower intestine was emptied by an enema, and an oral dose of magnesium sulfate was given each day. The dose of chlortetracycline was 2 gm. initially, followed by 0.5 gm. every six hours for the duration of the symptoms or to a maximum of one week. As patients in impending hepatic coma are sensitive to sedatives, these were avoided whenever possible. Drugs known to induce hepatic coma, such as ammonium salts, acetazolamide, and morphine, were not used. A common precipitant of hepatic coma is gastroesophageal hemorrhage, which increases the nitrogen content of the intestine. This was treated with a Sengstaken esophageal compression balloon. Of the 66 patients, 39 recovered; of these, 21 had been in deep coma. Sodium glutamate was given intravenously to some patients but without effect. In view of the extremely poor prognosis of hepatic coma treated by other methods, the authors believe that the protein-withdrawal treatment represents an advance. Some patients received low-protein diets for two years and maintained body weight and positive nitrogen balance.

Effect of Giving Live Influenza Virus.—Immunization against epidemic influenza is normally done by subcutaneous inoculation of virus inactivated by formaldehyde. Chick embryos are used for growing the virus. However, as there would not be enough fertile eggs available to supply sufficient inactivated virus in the event of a severe influenza epidemic, Isaacs and Roden, of the medical research council and the common cold research unit have tried inoculating volunteers with live influenza-A virus prepared by one amniotic passage and either 1, 4, or 10 allantoic passages in chick embryos. The inoculum contained between 10^4 and 10^6 egg-infective doses. The initial inoculation was done intranasally, but subsequently it was done by pharyngeal spray. Seventeen volunteers participated in four separate trials. No symptoms of respiratory infection developed; no virus was recovered from the volunteers; and no increase in serum antibody to the influenza antigen was observed. It was therefore concluded that the virus lost its ability to multiply in man and that this method would be unsuitable for mass immunization.

The items in these letters are contributed by regular correspondents in the various foreign countries.

Health in Ceylon.—A health survey published by the Ministry of Health of Ceylon reveals the advances that have been made in medical treatment and public health in only a decade (D. M. Silva, Health Progress in Ceylon, [illegible]). In seven years the general death rate has [illegible] it is 10.9 per 1,000, which is lower than that of Great Britain. Similarly, the infant mortality rate has been halved in the same period; it is now 71 per 1,000 live births. Maternal mortality has fallen to less than a third of the figure of seven years ago. These changes are not surprising in view of the large increase in expenditure for health services in Ceylon since dominion status was conferred on it in 1948. The expenditure per capita for health in 1945 was only three rupees; in 1953, it was 11 rupees. Health services have expanded, being partly aided by the World Health Organization and the Colombo Plan. One of the biggest contributions to public health has been the control of malaria, which until recently was responsible for more morbidity than any other disease. In 1946, there were 2,750,000 cases in Ceylon, or 412 per 1,000 population, with a death rate of 1.8 per 1,000. After 1947, all infected persons were treated and every habitation sprayed with chlorophenothane (DDT). In eight years the morbidity rate has been reduced from 412 to less than 5 per 1,000.

Tuberculosis is a severe endemic disease in Ceylon. Over 2 million of the population of 8 million have had a tuberculin skin test, and nearly a million negative reactors were given BCG vaccination. Mass miniature radiography, which was started in 1950, showed that 1% of all those examined had active tuberculosis. The death rate from this disease has been halved in the last three years, but ancylostomiasis still presents a problem and is responsible for more ill health than tuberculosis. A decade ago a third of the rural population was undernourished, not because of a shortage of food but because poverty prevented them from buying it. The lot is improving, but 16% of all school children still show signs of malnutrition. Cows are also undernourished, and this affects the quality and quantity of milk. The average yield per cow is only 60 gal., which is about a 10th that of a normal pasture-fed cow in Great Britain. The per capita consumption of milk in Ceylon is therefore only 2 oz. daily. The government issues free imported dried milk to about 250,000 people daily.

The improved health and nutrition services have resulted in a large increase in the population. The excess of births over deaths is now 28.5 per 1,000, compared with 4.5 in Great Britain; it is the highest figure in the world. This in itself presents a problem, because money must be found for more food, more schools, and more houses to keep pace with the rising population. This may make it difficult to find funds to maintain high standards of medical care, nutrition, and education. Large areas in the northeast of the island are being developed and made free from malaria; jungle areas are being cleared; and irrigation is being introduced. This may enable the island to support the increasing population.

Death of Obstetrician to the Royal Family.—Sir William Gilliatt, who was obstetrician to the Royal Family, died on Sept. 27 as a result of a traffic accident. He had been president of the Royal College of Obstetricians and Gynecologists and of the Royal Society of Medicine.

Cytological Diagnosis of Sex.—The claim of James (*Lancet* 1:202, 1956) that the sex of a fetus can be diagnosed from the examination of karyosomes in amniotic fluid cells has been confirmed by Sachs and co-workers (*Lancet* 2:795, 1956). They obtained amniotic fluid by puncture of the membranes and in the earlier months of pregnancy, with the exception of the third month, by abdominal puncture. The fluid was centrifuged, and the deposit stained on a slide with the Feulgen method, which is specific for desoxyribosenucleic acid. This is only present in the chromosomes and gives a clear staining of the karyosomes. The karyosome is longer in the cells of a female than of a male, and the percentage of cells with a karyosome at the nuclear membrane is greater. The figures are 4% in male cells and 38% in female cells. Dixon and Torr examined chromosomal sex differences in cells contained in oral smears (*Brit. M. J.* 2:799, 1956). Oral smears from 257 persons, representing a wide range of age and racial variation, were examined by Feulgen staining. In 162 male smears, no sex chromatin was seen, whereas, by contrast, in most of the 95 female smears between 30% and 50% of the cells counted contained a sex-chromatin mass. In the female smears, the sex chromatin was usually first seen in one of the first five cells counted. As this occurred with such regularity it was decided that a count of 25 cells from an oral mucosal smear was adequate for sex determination.

Histoplasmosis.—Prof. W. Symmers has described the first proved case of histoplasmosis in which infection was acquired in Great Britain (*Brit. M. J.* 2:786, 1956). Histoplasma capsulatum was isolated from a biopsy specimen taken from a patient who, like the other members of his household, had never been out of the British Isles. About a dozen cases have been reported in Great Britain, but, in each case, the patients had lived abroad in an area where histoplasmosis was endemic. In Symmers' patient, the only manifestations of the infection were enlargement of the cervical lymph nodes and a positive skin reaction to histoplasmin. H. capsulatum was found in cultures from one of the lymph nodes. No members of the patient's household reacted to intradermal histoplasmin, and the patient's hobbies and recreation did not expose him to any environment that has been incriminated as a source of infection.

Enzyme Tests for Detection of Glycosuria.—Hunt and co-workers reported on the use of glucose oxidase for the routine detection of glycosuria in diabetics (*Brit. M. J.* 2:586, 1956). The purified enzyme is now available commercially in testing preparations known as Tes-Tape and Clinistix. The former is a roll of test paper impregnated with glucose oxidase, *o*-toluidine, a vegetable peroxidase, and a yellow dye. When the strip is dipped into a liquid containing glucose, the oxidase in the presence of air converts it to gluconic acid and hydrogen peroxide, which with the peroxidase converts the *o*-toluidine into a blue oxidation product. This with the yellow dye gives a color, ranging from light green through dark green to dark blue, according to the amount of glucose present. A color scale is provided with Tes-Tape to indicate colors corresponding to 0, 0.1, 0.25, 0.5, and 2 gm. of glucose per 100 ml. of urine. Clinistix is a preparation in the form of separate strips of thick paper resembling book matches. No color scale is provided, as the test is purely qualitative. From tests on urine specimens from 174 diabetics known to be excreting glucose, from 43 patients excreting no glucose or only trace amounts, and from 46 normal subjects, it was concluded that both Tes-Tape and Clinistix are sufficiently accurate for the qualitative detection of glucose in urine. The limit of sensitivity is about 0.1 gm. per 100 ml. The advantage of these preparations is that no apparatus, boiling, or white tiles are necessary and that the test is specific for glucose; however, strict chemical cleanliness is necessary. Occasional false-positive tests were observed, but in no case did glycosuria go undetected. The authors are not satisfied that the preparations permit an accurate estimation of the amount of glucose present in urine. There was a significant difference in the amounts reported by different observers on the same urine specimens, and even greater discrepancies occurred when untrained observers read the results.

New Health Service Regulations.—The Minister of Health, after consultation with the representatives of the medical profession, has incorporated certain new regulations in the National Health Service code. These became effective on Oct. 1. The main amendments provide for (1) periodic reviews by executive councils of consents given to a physician to employ a permanent assistant; (2) a new procedure for identifying patients on a physician's list who are at a school or residential institution and, when they have gone away, for removing them from the list; (3) the abolition of back debits and back credits; (4) making a deputy to a physician responsible for his actions when both the deputy and the physician for whom he is deputizing are on the same medical lists; (5) enabling executive councils to make arrangements for the treatment of a physician's patients when he is absent or disabled; and (6) increasing the fee payable to a physician for the treatment of temporary residents at certain types of institution.

Overpopulation.—Overpopulation of the world, famine, disease, and disaster are not inevitable according to Dr. C. B. Goodhart, who addressed the annual meeting of the British Association for the Advancement of Science. Man's fertility may be lowered by natural selection. Families of lower fertility but otherwise good qualities are more likely to survive. In the British peerage, wealth in women is associated with infertility. An heiress by definition comes of a family of low fertility, for otherwise there would be siblings or other relatives to share her wealth. Many noble families have become extinct by the marriages of the sons to heiresses whose riches were as great as their infertility. The unattractive wife of King Louis XV of France had 10 children, whereas the attractive Mme. de Pompadour, his mistress, despite all her wishes, had only one child, who died young. Many other human characteristics leading to success in life are associated with low fertility; this, in turn, usually results in a higher standard of living. Population increase is primarily a biological phenomenon. The arguments of Malthus were based on the assumption that man had a specific and constant rate of reproduction, which would be the same in the future unless artificially altered. This assumption is not necessarily true. The present rate of increase in the population is quite exceptional. For 99% of his history, man lived as a nomadic hunter and food collector. The densely settled agricultural and urban communities characteristic of the last few millenniums are a relatively recent development. We cannot assume that the high fecundity found in these dense and unhealthy aggregations of population is necessarily typical of the human species. Declining numbers are found not only in primitive peoples brought into contact with civilization but also in many of the most advanced nations. The conditions produced by civilization and a high standard of living may in themselves be unfavorable to fertility. Those qualities leading to success in man may have become genetically correlated with relatively low fecundity.

Fertility in Scotland.—The *British Medical Journal* of Sept. 8 contains an annotation stating that, as a result of the steady fall in the birth rate from 316 per 1,000 married women in the period 1860 to 1862 to 132 in the period 1950 to 1952, the average size of families in Scotland has fallen from 6 to 2.5 children. The decline in childhood mortality has compensated for only part of the decline in fertility. The infant mortality rate is now 25% of the rate of 50 years ago, and the death rate for children under 10 years of age is about 12% of the rate of 50 years ago. A recent publication of the General Register Office, Edinburgh, presents statistics showing that almost 20% of all the married women in a random sample have no children and that only 0.6% have 10 or more children. The number of women at 23 years of age with no children and the number with one child are about equal. By the time a woman is 24 years of age, the average size of her family exceeds one child, but not until she is 32 years old does the average exceed two children.

For marriages under two years' duration, the number of childless women exceeds the number of women with one or more children. One-child families are the most frequent for women who have been married two to five years, but after six years of marriage the two-child families predominate. For marriages of the same duration, the average size of the family decreases with the increasing age of the mother at marriage. When analyzed by social class of the husband, the size of the family rises from an average of 1.48 for social class 1 to 2.58 for social class 5. There is a wide range in the average size of the family classified according to the occupation of the mother: for example, 70% of married clerks, typists, and office workers have no children, while only 12% of charwomen and office cleaners are childless. However, over half the women in the former group had been married for less than five years, while over half of those in the latter group had been married for 15 or more years. Geographical differences in the average size of the family are small: the rural areas have the largest families (average size about 2.11) and the small towns the smallest (1.90).

Streptococci on the Umbilicus.—The *British Medical Journal* of Sept. 8 contains an article by Drs. Boissard and Eton and another by Drs. Kwantes and James who simultaneously conclude that many hitherto unexplained outbreaks of streptococcic infections in maternity hospitals can be traced to an umbilical source, and they make the plea that bacteriological investigation of the nursery should be carried out whenever a case of streptococcic infection is found in a mother or a member of the staff. There was no local sign of any infection in most of the infants whose cords were found to be infected. It is not surprising that the stump of the cord, consisting of dead tissue undergoing dissolution, should support the free growth of bacteria. What is surprising is that an infant with no acquired immunity and with only a few days' experience with bacteria of any kind should be able to keep virulent streptococci in check at the junction of dead and living tissue. These observations nevertheless show that the umbilicus can be a symptomless reservoir of such infection. Contaminated in the first instance probably by a nurse, it can evidently be the source from which the mother acquires a uterine infection and from which other babies in the ward acquire an umbilical infection. One effect of these findings must be that umbilical swabs be regularly included in those taken to determine the source of infection in puerperal fever.

No More Overtime in Mental Hospitals.—More than 26,000 male and female nurses in mental hospitals refused to work overtime after Oct. 1. The ban must worsen conditions already bad because of overcrowding and a shortage of staff workers. A last-minute effort to avert this will be made. The decision to ban overtime was taken by a vote of 399 to 381 and will continue until the demands of the Confederation of Health Service Employees are met in full. These include higher ordinary and overtime pay; a 44-hour week; and six weeks' annual leave, including bank holidays and weekly leaves. A 96-hour fortnight is the rule in both mental and general hospitals. The Industrial Court has rejected the confederation's request that overtime after 96 hours should be paid for at time and a quarter for the first two hours and time and a half thereafter. At present, overtime is paid for at the ordinary rate. Much overtime is worked and is popular with many employees as an additional source of income. Nurses commonly work 60 to 70 hours a week; many have broken down under the strain. Others have forsaken mental health work for other forms of nursing. Dissatisfaction is general throughout the service. The secretary of the confederation emphasized that no patient would be left uncared for because of the ban. Nurses will not be required to leave patients needing attention until a relief has arrived. While patients will not lose nursing care, they will be deprived of such things as entertainment, because no one will be available to supervise.

Eyeglasses Without Examination.—The harmful effects of eyeglasses bought in shops without an ophthalmologic examination or professional advice are being investigated. Results of the inquiry will be reported to the Minister of Health. Shop sales of glasses dwindled almost to nothing after the introduction of the National Health Service, which made it possible to obtain glasses free. However, since May, 1951, people have had to pay $2.80 and the cost of the frames. Again there is much indiscriminate buying. Glasses can be bought for as little as 28 cents a pair. Among those who buy their glasses from shops and peddlers are many old-age pensioners. Concern about increasing shop sales of eyeglasses was expressed in a resolution submitted at the Labor party conference in October that urged that plans be prepared for the next Labor government to stop this practice and reintroduce free glasses. The Guillebaud Committee on the cost of the National Health Service, in its report last January, recommended that, when it could be afforded, a substantial reduction in the charge for glasses should be given high priority.

THE LEISURE CORNER

SKIING AS WEEK-END RECREATION

"Travels in the mountains undertaken in the company of friends are the highest of all pleasures and the most charming of all delights of the senses are obtained. . . ." So wrote Conrad Gessner, physician of Zurich, Switzerland, in 1555. The peripatetic doctor did not mention skis as the model mode of "travels in the mountains," but it can be safely assumed he might have had them in mind, since men have used skis to journey in mountains for more than 4,500 years.

At any rate, millions of Americans, 400 years later, are taking the Swiss doctor's remarks to heart. Every week end, from November through April, depending on the weather, of course, the highways are filled with automobiles carrying skiers, young and old, to the snow-covered slopes; railroad stations resound to the joyful and enraptured shouts of athletes, aged 20 to 60, carrying skis and rucksacks like so many gay, brilliant banners.

These are the week-end athletes—office boy and office manager, factory hand and plant foreman, salesman and store executive—released by the shorter work week from the shackles of their jobs for long week ends. Two days a week they can be found shackled to two slim wooden boards, racing up and down snow-covered slopes to steep inclines with the abandon that is the distinguishing characteristic of their sport. Dangerous? A little, perhaps, but not so bad as a treacherous undertow or a fall from a horse, is the skier's retort. Difficult? Anything that can be learned on week ends, not necessarily consecutive, is not hard. Rugged? Persons in their 50's have been known to take up the sport for the first time and stay with it in their 60's.

Week-end athletes, of course, suffer one drawback—the uncertainties of the weather. In the summer they repeat the intonation of their childhood: "Rain, rain go away, come back another day." In the colder weather they look longingly to the skies for the gray clouds that spell the advent of snow. Physicians who can get away for several weeks at a time have a much better chance of ascertaining the truth of their ancient colleague's observation. Once they get the taste, the chances are they will become week-end athletes too. And since there are no age limits, skiing can become a family affair. Wife and children can easily fit in "the company of friends" to guarantee "the highest of all pleasures."

Mountains need not be high or overly rugged; sites are available for individual tastes and peace of mind. The only requisite is the desire. And as for the last, there is only one note of caution: once you get the desire, you never lose it. Nor need skiing be an expensive sport. It is only if you want it to be. However, it is not wise to stint on good equipment; poor equipment can be false economy.

Most important ingredients of your outfit are boots and bindings, since they are the links between skier and ski. Put on thick woolen socks before trying on the boots to make sure the boot will fit properly. Some ski experts even insist that you bring along your own socks for the fitting to make certain the boots will not feel too snug. As for the bindings, all-metal ones are considered the best, although some experts recommend a good grade of leather straps for beginners.

Skis, almost everyone agrees, should be of hickory wood. Other woods are unsatisfactory for various reasons, and metals and plastics have not been sufficiently tested to have won wide acceptance. Some experts say a ski must reach to the base of your thumb when you stand them erect; others insist weight must be considered. The latter advise a ski somewhat shorter than the base-of-thumb length. Good ski poles should reach from boot to armpit and be made of metal tubing or tonkin cane. Well-padded hand grips and good leather wrist straps are important.

Ski clothing generally is a matter of individual taste, but here the experts also have a word of caution. Designers for one of the foremost makers of ski clothing in the country advise that pants and jackets should be well fitted and tapered, yet full cut to permit freedom of movement. They say loose-fitting pants, for instance, tend to cause wind resistance. The material should be closely woven, smooth, and snow-repellent. Do not make the mistake of buying ski clothing for warmth, the experts add. Undergarments will supply warmth, but you must make sure they do not supply too much bulk as well. Then there are such incidentals as goggles, wax, mittens, sunburn preventives, and other items that individual skiers may like. Most of them are necessary, but none are too expensive.

Different conditions prevail in different parts of the country, which means that skiing techniques may vary from place to place. But no one has to become an expert in any or all types of skiing to enjoy the sport. No matter what time of life you begin, you have the rest of your active span of life to improve both style and technique—if you care, or if you have any style or technique to improve.

Of course, there are certain fundamental skills to learn. One school promises to teach skiing in a week. Whether you are interested in the Swiss school, or the Arlberg, or the Norwegian, or the American, it does not matter. Fundamentally there is one system of skiing. All schools are based on the snowplow or the snowplow turn. In the snowplow your skis form a reverse V to brake your momentum; in the snowplow turn, you turn right by shifting weight to the left ski, and left by shifting to the right ski. And above all, no matter what the school, the system, or the technique, you must learn to relax.

Since relaxation and leisure are inseparable, like ski and boot, what better way of combining both than by skimming through the dustless air of higher altitude, over the bluish luster of virgin snow, through wooded trails, enjoying the long, slow rhythm of great sweeping turns or knowing the enormous spray of powder snow thrown up by a jerked Christiania. And through it all courses the ecstasy and the strange intoxication of swift passage through the keen, sharp, clean, tangy atmosphere. Slalom!

MEDICAL FILM REVIEWS

Fractional Lumbar Epidural Analgesia: 16 mm, color, sound, showing time 12 minutes. Prepared by LeRoy W. Krumperman, M.D., Philadelphia. Produced in 1956 by Audio Productions, New York, for Sharp and Dohme Division of Merck and Company. *Procurable on loan from* LeRoy W. Krumperman, M.D., 3401 N. Broad St., Philadelphia 40.

The purpose of this film is to show a practical technique of performing lumbar epidural analgesia. The contents of the epidural tray are shown and described, and the value of this technique of regional analgesia for surgery as well as or a diagnostic and therapeutic block is pointed out. The technique of identifying the epidural space by using the "drop-sign" of Gutiurez is shown; also shown is the introduction of a polyvinyl catheter through the needle into the epidural space. By anatomic drawings, the film shows the proper position of the needle in the epidural space and also the polyvinyl catheter in the epidural space. The indications and contraindications for this form of regional analgesia are described, and there is also a comparison made between epidural and spinal analgesia, with the advantages and disadvantages of each technique pointed out. The over-all film is good; however, the advantages and disadvantages of other drugs and the other techniques for locating the epidural space should have been mentioned. The hazards of and the preparation for a reaction to a local anesthetic should have been discussed. The photography is good, and the film is recommended for surgeons, anesthesiologists, and members of hospital house staffs.

Dynamics of the Tubercle: In Vivo Observation of Pathogenesis and Effects of Chemotherapy in the Clark Rabbit Ear Chamber: 16 mm, color, sound, showing time 28 minutes. Prepared by Robert H. Ebert, M.D., and William R. Barclay, M.D., University of Chicago. Produced in 1956 by Churchill Wexler *Productions*, Los Angeles, *for and procurable on loan from* Pfizer Laboratories, Chas. Pfizer and Co., Inc., Brooklyn 6, N. Y.

This excellent film shows the effect of the introduction of disease in normal tissue and the results of chemotherapy upon the disease. The early part of the film explains normal circulation in the rabbit ear and describes in detail progressive changes in the normal vessels, blood cells, and connective tissue after the introduction of the tuberculosis organisms in a primary infec tion and also the development of the tubercle in reinfectio tuberculosis. The latter part of the film shows the effects o chemotherapy on the tubercle. This is an excellent teaching fil for histology, physiology, and pathology, since it demonstrat (1) normal tissue, (2) the result of introduction of infection i normal tissue in the primary stage and reinfection stage, an (3) the effect of chemotherapy on the evolution of the infectio This film should be used not only in all medical schools b also in schools of nursing and as a part of the educational pro ess of science students at the college level.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Dissecting Aneurysm of the Aorta with Neurological Involvement. E. N. Weaver. Virginia M. Month. 83:431-437 (Oct.) 1956 [Richmond, Va.].

The author describes five cases of dissecting aneurysm of the aorta in four men between the ages of 33 and 64 years and in a 55-year-old woman. Each of these patients had neurological changes consisting in four of paralysis of the lower extremities, right hemiparesis and a right homonymous hemianopsia, weakness and numbness of the right leg, and weakness of both legs respectively. The neurological changes, which were produced by ischemia of some part of the nervous system as a result of the aortic dissection, emphasized the dominance of neuropathology as the basis of the patients' symptoms. A dissecting aortic aneurysm should be considered in patients who experience sudden severe and unexplained chest, abdominal, back, or leg pain with bizarre radiations and associated neurological signs and symptoms. All five patients died, and autopsy was performed in four. Death occurred as a result of rupture of the aneurysm into the pericardium, the thoracic cavity, or the abdominal cavity. One patient had repeated ruptures and lived for almost five months from the time of onset of his illness. The importance of developing a clinical consciousness of this condition with early diagnosis is emphasized, since many of these lesions are amenable to treatment.

Clinical Consideration on Arterial Embolism and Valvular Misfunction. G. Micheli-Pellegrini and P. R. Lapi. Sett. Med. 44:344-349 (July 15) 1956 (In Italian) [Florence, Italy].

The authors studied arterial embolism in 895 cases of rheumatic valvular disease of the heart. Embolism was found in 38 patients (4.2%). Twenty-nine patients had cerebral embolism, 19 on the right side and 10 on the left side. Two had it in the left arm, one in the right arm, two in the bifurcation of the common iliac, four in the left leg, one in the right leg, and one in the mesentery. The patients were mostly between the ages of 40 and 50 years. There were 33 women and 5 men. It is possible that endocrinal and vegetative factors, the balance of which is less stable in women than in men, may play an important role in causing embolism. Physiological changes in genital function seem to influence the general course of heart disease. The authors noticed in the past history of five patients that the detachment of the embolus coincided with the premenstrual period. Arterial embolism was noticed mainly in patients with valvular mitral disease. Autopsy in five patients showed severe mitral stenosis. Embolism rarely occurred in the first 15 years of the heart disease. Bouillaud's disease was the type of rheumatic disease chiefly responsible for valvular misfunction.

A Study of Serum Lipoproteins in Normal and Atherosclerotic Patients by Paper Electrophoretic Techniques. W. P. Jencks, M. R. Hyatt, M. R. Jetton and others. J. Clin. Invest. 35:980-990 (Sept.) 1956 [New York].

Studies were made to test the large-scale application of two relatively simple methods for the estimation of electrophoretically separated serum lipoproteins by measurement of their cholesterol content and dye-binding capacity. The results of these two methods were compared with each other and with ultracentrifugal methods, the aim being to obtain further confirmation of the association of serum lipoprotein abnormalities with atherosclerosis. Both healthy and hospitalized control groups were used to lessen the possibility that any observed abnormalities might be the result of illness, medication, diet, or restricted activity rather than of atherosclerosis *per se*. A standardized technique for the estimation of serum lipoproteins separated by paper electrophoresis gave results comparable to those of cholesterol determinations on these liproproteins and of ultracentrifugal analysis of lipoproteins at a density of 1.21. No appreciable difference in lipoprotein concentration or distribution, measured by paper electrophoretic techniques, was found between the serums of 68 healthy male Army officers and the serums of 65 patients hospitalized with diseases not associated with atherosclerosis or abnormalities in lipid metabolism. Analyses of serums from 77 men with atherosclerosis, as judged by a history of myocardial infarction, showed a significant drop in alpha lipoprotein and increase in beta lipoprotein, resulting in a decreased ratio of alpha to total lipoprotein in these serums as compared to those of the control groups. Elevations in total cholesterol and total lipid dye-binding capacity were less significant. The percentage of the total serum cholesterol in the alpha lipoprotein fraction was lower in serums from patients studied from zero to six months than in those studied more than six months after an acute episode of myocardial infarction. The electrophoretic distribution of serum proteins showed greater deviations from normal in the group of hospitalized patients than in the atherosclerotic group. Ultracentrifugal analysis of lipoproteins of Sf 12-20 were less often abnormal than were electrophoretic analyses of the ratio of alpha to total lipoproteins in serums from atherosclerotic patients.

Gastric Ulcers: Review of 100 Cases. J. H. Geddes, W. N. Downe and J. A. Taylor. Canad. M.A.J. 75:550-554 (Oct. 1) 1956 [Toronto, Canada].

One hundred patients with gastric ulcer were treated at the Westminster Hospital in London, Ontario, between 1946 and 1952. Thirty patients were treated surgically and 70 were treated medically. The reasons for operation in the surgically treated patients were suspected malignancy in 14, recurrent ulcer in 13, and hemorrhage in 3. With the exception of six, all had subtotal gastrectomies. Only one of the 30 patients treated surgically was found to have carcinoma of the stomach. All medically treated patients were followed up for from two to seven years and none of them had any evidence of gastric malignancy. Twenty of the 100 patients have died since the diagnosis of gastric ulcer was made, and none of them died of gastric neoplasm. These results seem to vindicate the authors' present method of treatment for gastric ulcers, consisting of three to six weeks of intensive medical management in hospital in an attempt to arrive at an opinion concerning the question of malignancy of the ulcer. Clinical and radiological evidences of healing were considered the most important factor in deciding the nature of the ulcer. Other aids employed were the degree of gastric acidity, gastroscopic appearance, and cytology of gastric washings, when available. At the end of three weeks patients were again examined roentgenologically, and if healing was complete the ulcer was considered benign. If healing was incomplete, medical treatment was continued for three more weeks, followed by another barium meal. If the latter showed continued evidence of ulceration, the ulcer was considered malignant and surgery recommended. All patients with ulcers deemed benign were advised to have a barium meal every three to six months for two years.

It would appear that, with careful evaluation of a gastric ulcer in a patient hospitalized for a period of from three to six weeks, an error of 3% or less can be expected. Partial gastrectomy, the surgical treatment of choice for gastric ulcers, has a comparable mortality rate and in addition a definite morbidity of 10%. It is concluded that treatment of patients with gastric ulceration should be individualized, that surgery is not warranted for all patients with gastric ulcer, and that as a rule it should not be carried out before an earnest and careful attempt

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has been made to determine whether benignity or malignancy exists. Surgery should be carried out as soon as possible in all patients with recurrent ulcer, ulcer on the *greater curvature*, pyloric obstruction, hemorrhage, and perforation.

The Superior Vena Caval Syndrome: Report of 21 Cases. E. A. Calkins. Dis. Chest. 30:404-411 (Oct.) 1956 [Chicago].

Twelve men and nine women between the ages of 41 and 83 years with superior vena caval obstruction were admitted to the Los Angeles County General Hospital between 1947 and 1954. Clinical evidence of superior vena caval obstruction consisted of swelling of the neck, face, and arms and extensive venous collateral circulation over the chest and abdomen with downward flow of blood. In addition, 9 of the 21 patients had shortness of breath and cyanosis of the upper extremities. Arm venous pressure readings were obtained in eight patients with a range of from 250 to 800 mm. sodium chloride solution and an average of 386 mm. Only four pressure readings were obtained from the patients' lower extremities, showing an average of 165 mm. with sodium chloride solution. Arm-to-tongue circulation time averaging 34 seconds was determined with the aid of dehydrocholic acid (Decholin) in six patients. Arm-to-lung time averaging seven seconds was determined with the use of ether in three patients. In four patients angiograms illustrated superior caval or innominate obstruction. The superior vena caval syndrome was caused by bronchogenic carcinoma in 11 patients, by aortic aneurysm in 2, by substernal thyroid in 2, and by undiagnosed mediastinal tumors, nodes, or granulomas in 6. Fifteen patients died, 11 as a result of bronchogenic carcinoma. Six with remission of symptoms or no progression were discharged.

A review of the literature suggests that the major causative factor is bronchogenic carcinoma, which may involve the superior vena cava in from 10 to 15% of the patients, with a generally unfavorable prognosis. With increased knowledge and use of vessel grafting the prognosis is brighter for those in whom the obstruction of the superior vena cava is not caused by a malignant tumor or an aortic aneurysm. Some definite trends were noticed in the author's small series of cases. In contrast to the reports in the literature the predominance of men in the ratio of men to women was reduced from 75% to 57%. The age of the patients appeared to increase and so did the incidence of bronchogenic carcinoma as a causative factor. The average venous pressure in the arms may exceed that in the legs by more than 200 mm. sodium chloride solution.

I^{131}-Labeled Fat in the Study of Intestinal Absorption. J. M. Ruffin, W. W. Shingleton, G. J. Baylin and others. New England J. Med. 255:594-597 (Sept. 27) 1956 [Boston].

Characteristic and reproducible curves of blood levels of radioiodine (I^{131}) have been demonstrated with the use of both radioactive-tagged albumin and radioactive-tagged fat. This method of study was applied to patients with a variety of disorders of the gastrointestinal tract to determine whether their radioactive blood levels and fecal content differed significantly from those found in normal persons. A cold emulsion and a "hot" emulsion were prepared. The cold emulsion consisted of 200 ml. of peanut oil, 200 ml. of water and 15 ml. of Tween 80. The "hot" emulsion consisted of 45 ml. of peanut oil, 5 ml. of I^{131}-labeled glycerol trioleate (2.0 mc. of I^{131}), 50 ml. of water, and 4 ml. of Tween 80. Each emulsion was prepared by mixing of the ingredients in a Waring blender for 15 minutes. Each patient, in a fasting state, was given a test meal consisting of the following: the volume of "hot" emulsion that contained 25μc of I^{131} to which was added enough cold emulsion to make a total of 1 ml. per kilogram of body weight. Twenty grams of barium sulfate was added to the test meal, and the entire contents mixed. The subject drank the test meal. The container was rinsed twice with 50 ml. of tepid water, which was likewise ingested. The container was assayed for residual I^{131}. Twenty drops of Lugol's solution was given immediately after the test meal. Two milliliters of venous blood was withdrawn at hourly intervals for six hours after ingestion of the test meal. Each sample was placed in a separate tube and assayed for I^{131} content in a scintillation crystal-well counter.

The 180 patients tested with the labeled fat included 44 with functional gastrointestinal disturbances; 57 with gastrointestinal diseases (including pancreatitis, carcinoma of the pancreas, sprue, enteritis, colitis, and hepatic cirrhosis); and 79 who had been operated on for peptic ulcer. In the group of patients with functional gastrointestinal disturbances, the blood levels and fecal excretion were within normal limits, while patients who had disease of the small intestine, regardless of cause, invariably had profound lowering of their blood levels and marked increase in radioactive content of the stool. The patients with sprue in clinical remission had completely normal blood and stool values, pointing to the reversibility of the pathological process. Patients with disease of the colon only had normal absorption. This was also true of patients with cirrhosis of the liver. The evidence in patients with disease of the pancreas points to faulty digestion rather than to an intrinsic error of absorption: 12 of the 13 patients with carcinoma of the pancreas had abnormal levels. Fifty-three per cent of the patients who had undergone gastric surgery for peptic ulcer showed significant lowering of the blood curves and increase in radioactive content of the stool. It is well known that appreciable weight loss is fairly common in postresection and postvagotomy patients; these findings suggest that one of the factors causing weight loss in this group of patients is impaired fat absorption.

Superior Vena Cava Draining into Left Atrium: Another Cause for Left Ventricular Hypertrophy with Cyanotic Congenital Heart Disease. H. Tuchman, J. F. Brown, J. H. Huston and others. Am. J. Med. 21:481-484 (Sept.) 1956 [New York].

A 15-year-old boy was hospitalized in February, 1955, complaining of fatigue and unexplained fever. In October, 1954, his physician had found that polycythemia was present. In February, 1955, the patient appeared to be moderately plethoric with cyanosis of the acral parts. Down-curving of the finger nails without actual clubbing was noted. The conjunctival and retinal vessels were engorged. The left border of cardiac dulness was at the midclavicular line. The liver was palpable 3 cm. below the costal margin, and the spleen was just palpable. Cardiac catheterization revealed a superior vena cava that drained into the left atrium. The impression was that the patient had a single vascular anomaly in which the superior vena cava entered directly into the left atrium. Surgical exploration confirmed this. The aorta and the left ventricle were enlarged. The right atrial appendage was hypertrophied and dilated. Within the pericardium and extending upward from the cephalic end of the right atrium was fibrous remnant of the normal superior vena cava. The patient died 20 hours after the operation.

Postmortem examination confirmed the diagnosis and failed to reveal any other congenital cardiac anomaly. The case is thought to be of interest because it represents another type of cyanotic cardiovascular anomaly producing left ventricular hypertrophy and because the quantity of shunt as calculated here confirms the existing impression that about one-third of the venous return is via the superior vena cava and about two-thirds via the inferior vena cava. The diagnosis should be easily available to all who have access to cardiac catheterization and angiocardiography, and correction by surgery is feasible.

Episodic Stupor Following Portacaval Shunt: Observations on Etiology and Therapy. C. J. Fisher and W. W. Faloon. New England J. Med. 255:589-594 (Sept. 27) 1956 [Boston].

A 58-year-old man was first hospitalized with hematemesis, and a diagnosis of portal cirrhosis with bleeding esophageal varices was made. He had a history of chronic alcoholism associated with a poor dietary intake for many years. A splenorenal shunt was performed. Six months later he was readmitted with gastrointestinal bleeding, and x-ray study again revealed esophageal varices. A portacaval shunt was performed. Twelve episodes of coma or deep stupor were observed in this patient. They could be related to intolerance to more than 25 gm. of dietary protein ingested orally, to protein hydrolysate infusions, or to oral administration of ammonium chloride. The sequence of the development of coma included the stages of flapping tremor of the outstretched extremities, usually associated with mental confusion, gradually increasing stupor, and coma. During recovery the sequence of events was reversed.

His mental status, even when he was "alert," was markedly abnormal. No clear-cut correlation between the clinical condition and the venous-blood ammonia levels was observed. Neomycin therapy resulted in marked reduction in blood ammonia levels and enabled this patient to ingest a regular hospital diet containing approximately 90 gm. of protein.

Stable and Brittle Diabetes. J. G. Alivisatos and E. P. McCullagh. Am. J. Med. 21:344-357 (Sept.) 1956 [New York].

There are patients with long-standing diabetes in whom the blood sugar values are consistently fluctuating, in spite of attempts to obtain normoglycemic control, and who nevertheless have only very slight degenerative complications. The authors believe that this is due to uncertainties as to definition of the term "control" and to the failure to recognize the existence of two distinct types of diabetes mellitus, the stable and the brittle. They apply the term stable diabetes to patients who are insulin-insensitive and brittle diabetes to those who are insulin-sensitive. Another distinct metabolic feature of patients with brittle diabetes is that ketosis develops rapidly and repeatedly despite attempts to establish normoglycemic control. If insulin is not administered in adequate doses, diabetic coma will develop. Ketosis indicates increased catabolism of fat. These disturbances in the carbohydrate and fat metabolisms in patients with brittle diabetes suggest that this type of diabetes is a separate metabolic entity. This study was undertaken to ascertain whether or not other clinical or biochemical features distinguish brittle from stable diabetes and whether the incidence of late degenerative complications is different in these two groups of patients. One hundred seventy-two patients were studied, but only 149 fulfilled all the criteria for classification in one or the other of the two groups. There were 70 patients with brittle diabetes and 79 with stable diabetes. When distribution curves of the over-all blood sugar values were plotted, it was found that patients with brittle diabetes had a V-shaped curve indicating that these patients have a high frequency of blood sugar values in the two extreme ranges, the very low (less than 120 mg. per 100 cc.) and the very high (above 200 mg. per 100 cc.). In patients with stable diabetes the blood sugar curve is a descending line. Degenerative complications were more frequent in patients with stable diabetes than in those with brittle diabetes. The incidence of severe diabetic retinopathy was low in adult patients with brittle diabetes of long standing. Patients with stable diabetes with poor control showed a significantly higher incidence of late degenerative complications than patients with stable diabetes with good control.

Treatment of Severe Tetanus with d-Tubocurarine Chloride and Intermittent Positive-Pressure Respiration. A. C. Smith, E. E. Hill and J. A. Hopson. Lancet 2:550-552 (Sept. 15) 1956 [London, England].

Intermittent positive-pressure respiration in association with some method of preventing spasm is an advance in the treatment of severe tetanus. The patient presented, a 7-year-old boy, had an especially severe form of tetanus. He had been cut on the forehead by a sharpened stick used as an arrow. His doctor treated the wound, which was superficial, but gave no antitetanic serum because of an allergic reaction to a dose of serum given 18 months before. The wound became infected and was treated with penicillin and aureomycin. Four days after the injury the right side of the patient's face became stiff and trismus developed. The patient was treated for 26 days with paralysing doses of curare (up to 640 mg. in 24 hours to a total dose of 7,640 mg.), and respiration was maintained by intermittent positive pressure from a Radcliffe respiration pump. Chloral hydrate was given to prevent any memory of the period. The patient made a complete recovery.

The d-tubocurarine was chosen as the relaxant for two reasons: 1. Absolute muscle relaxation can always be obtained if enough curare is given. 2. Curare has been successfully used in other cases. The standard dose of curare in this patient was 15 mg. given intravenously, and this dose abolished all muscular movement for a time. Spasms, modified to myoclonic twitching, recurred after from 20 to 30 minutes, and more curare was given when these spasms became obvious. The authors gained the impression that the occurrence of even these modified spasms adversely affected the patient's general condition, and they would probably be even more lavish with the dosage of curare in a future case. The diet was based on an intake of 72 oz. of milk daily with additional glucose and Casilan to provide 1,750 calories. The high-protein diet usually given to these patients was not given, because this patient's blood-urea level never fell below 50 mg. per 100 ml. The patient's voracious appetite after normal feeding was resumed suggests that this calorie intake was insufficient. Penicillin and streptomycin were given for the first week against the causal organism and prophylactically against chest complications. Sulphadimidine in small doses was given for the rest of his illness and, in association with physiotherapy and changes of posture, controlled his chest infection. Promethazine was given to minimize allergic reactions.

Infection of Volunteers by a Virus (A. P. C. Type 1) Isolated from Human Adenoid Tissue. A. T. Roden, H. G. Pereira and D. M. Chaproniere. Lancet 2:592-596 (Sept. 22) 1956 [London, England].

A strain of type 1 APC (adenoidal-pharyngeal-conjunctival) virus was administered by nasal instillation to 11 volunteers. Garglings taken on the second, fourth, and sixth days after the instillation were examined for the presence of type 1 virus, which was recovered from none of the volunteers on the second day and from four of them on the fourth or sixth day. Acute pharyngitis developed on the fourth and fifth days in two of the volunteers from whom the virus was recovered. The remaining volunteers showed no clinical signs of infection. Paired serums were tested for neutralizing and complement-fixing antibodies for APC viruses of tyypes 1 to 6. Neutralizing antibodies for type 1 virus were not detected in the preadministration serums of any of the four volunteers from whom the virus was subsequently recovered but were present to varying titers in the preadministration serums of the remainder. All volunteers from whom the virus was recovered showed definite increases in neutralizing antibodies for the homologous type and variable responses to the heterologous types. Three volunteers from whom no virus was isolated showed increases in neutralizing antibodies. Rises in complement-fixing antibodies were observed only in the group of volunteers from whom virus was recovered and were greatest in the two volunteers who showed clinical evidence of infection.

Polycythemia and Hypernephroma. E. Noe. Nord. med. 56: 1164-1165 (Aug. 18) 1956 (In Norwegian) [Stockholm, Sweden].

In eight of the nine previously published cases of polycythemia and hypernephroma the finding of hematuria made possible the diagnosis of renal tumor during life. In the three patients operated on the polycythemia disappeared after nephrectomy. The polycythemia is thought to be secondary to the renal tumor. There is no clearly formulated theory as to the mechanism in this connection. In the case reported, in a man aged 55 with pleural exudate, there were no symptoms from the urinary tract to indicate urography. The diagnosis of polycythemia was based on the hemoglobin, red blood cell, and thrombocyte values, together with the typical sternal punctate. Cerebral symptoms that set in were ascribed to cerebral thrombosis, and anticoagulant treatment was applied. The patient died in coma and hyperthermia. Autopsy revealed a tumor of the right kidney and tumors of similar appearance in the right pleura and right cerebral hemisphere. The microscopic picture showed hypernephroma. The pleural exudate proved to be an expression of pleural metastasis of the hypernephroma.

Pneumoperitoneum in the Management of Esophageal Hiatus Hernia: A New Diagnostic and Therapeutic Procedure. B. Masel, W. Cooper and F. Glenn. J. Am. M. Women's A. 11:299-315 (Sept.) 1956 [New York].

Pneumoperitoneum was used as a new diagnostic and therapeutic procedure in five patients with esophageal hiatus hernia. The pneumoperitoneum established the differential diagnosis between angina from coronary arterial insufficiency and angina produced by hiatus hernia and also between dyspepsia caused by gallbladder disease and dyspepsia due to hiatus hernia. The pneumoperitoneum controlled hemorrhage, vomiting, rumination, and dyspepsia caused by hiatus hernia. It is induced in the following manner: The patient is placed in the supine position. The abdomen is shaved and prepared with three applications of zephiran. A point midway between the left costal margin and the umbilicus is infiltrated with 2% procaine solution. A 19-gauge needle, 1.75 in. long, attached to a 10-cc. syringe, is introduced into the abdominal wall to a point where the anterior rectus sheath is encountered. A needle guard or a clamp is adjusted to the needle to permit safe advancement for another 1.5 cm. through the rectus muscle, the posterior rectus sheath, and the peritoneum. As the needle passes through the peritoneum, the patient feels a slight sticking pain. Five cubic centimeters of novocain is introduced into the peritoneal cavity to test the free flow and to make certain that the needle tip is within the peritoneal cavity. A three way stopcock is attached, and small amounts of room air are introduced to test the free flow into the peritoneal cavity. The 10-cc. syringe is replaced by one that holds 50 cc., and about 1,000 cc. of air is injected. Codeine phosphate is given every four hours for four doses to control the shoulder pain caused by the air beneath the diaphragm.

The peritoneum proved of particular value in aged patients with hiatus hernia. It did not produce recognizable interference with the cardiopulmonary function and did not complicate the operative management of these patients. On the contrary, the great amount of space beneath the stretched and elevated left diaphragm facilitated the repair of the diaphragm and the manipulation of the stomach, esophagus, spleen, and left lobe of the liver. Hiatus hernia may cause left flank pain, clinically indistinguishable from renal pain. The elderly patient with a symptomatic hiatus hernia may be treated on an ambulatory basis in a hiatus hernia pneumoperitoneum clinic, provided the initial injection of air is given in the hospital under close supervision. The clinical course and the signs, symptoms, diagnosis, and pathological changes of esophageal hiatus hernia are reviewed. The authors suggest that the development of paraesophageal and sliding hiatus hernia can be attributed to the loss of the normal vis-a-tergo of the tissues at the esophageal hiatus and the effects on the stomach of a rising and falling intrathoracic pressure associated with coughing, sneezing, and defecation. Hiatus hernia is often associated with chronic cholecystitis, cholelithiasis, and peptic ulcer.

Treatment of Uremic Nausea and Vomiting with Chlorpromazine (Largactil). P. Eilersen. Ugesk. læger. 118:953-954 (Aug. 16) 1956 (In Danish) [Copenhagen, Denmark].

In Bispebjerg Hospital intractable nausea and vomiting in 21 patients with uremia due to chronic nephritis, nephrosclerosis, or chronic pyelonephritis were treated by peroral administration of Largactil. The dosage was 25 mg. four times daily except in two instances, in which the dosage was 50 mg. four times daily. The symptoms ceased in nine patients, five were improved, and in seven there was no change. Two of the nine patients had been greatly troubled by hiccups, which ended at once on the Largactil treatment. The appetite was improved in all the improved patients. In spite of subjective improvement, the blood urea level was not reduced during the period of treatment. Nine patients with cancer metastases and four with other diseases were also treated with chlorpromazine because of nausea and vomiting. In four of the first group the symptoms disappeared entirely, while three were improved and two unchanged; in three of the second group the symptoms ceased, and the fourth patient was improved. While no side-effects of chlorpromazine were seen, the substance should, on account of the side-effects described in the literature, be reserved for the treatment of continuous nausea and vomiting in incurable patients.

Herpes Zoster and Liver Diseases. W. Siede. Deutsche med. Wchnschr. 81:1401-1402 (Aug. 31) 1956 (In German) [Stuttgart, Germany].

Siede reports on seven patients in whom herpes zoster occurred in association with liver disorders. The liver was more or less enlarged and its consistency increased in all seven patients. Liver biopsy in two patients revealed the histological characteristics of involvement of the hepatic mesenchyma, with proliferation and chronic inflammatory infiltration of the periportal tissues. This process also involved some of the peripheral lobules. The stellate Kupffer's cells were increased. The hepatic cells showed a granular or vacuolated protoplasm, and here and there a cell membrane and nuclear synthesis. The protein tests indicated pathological changes, and electrophoresis revealed a constellation of the protein fractions characteristic of hepatic impairment. Liver-function tests carried out during the acute stage also indicated a pathological condition. Only one of the patients was definitely jaundiced, but three were subicteric. In five of the patients the hepatitis subsided within weeks; in one it persisted for eight months; and the seventh still has signs of chronic hepatitis after two years.

Herpes zoster is apparently an infectious disease caused by a virus. The question arises whether the concurrence of herpes zoster and hepatitis in the cases presented was fortuitous or whether there was an etiopathogenetic relationship. In some of the patients the herpes zoster appeared in the segments that correspond to the sympathetic innervation of the liver. This might suggest that the virus hepatitis produced a site of lessened resistance; however, this would presuppose that the hepatitis preceded the herpes zoster, and this occurred in only one of the patients, whereas in the others the appearance of the two disorders coincided. The author believes that both diseases can be caused by the same virus. A number of virus diseases are known to cause disorders in several organ systems. As a typical example he mentions glandular fever, which involves not only the lymphatic apparatus but occasionally also the liver and the central nervous system. The same applies to primary atypical pneumonia. More recently it has been observed that the virus diseases of the central nervous system may show the same behavior. Thus, involvement of liver and spleen and even hepatitis with jaundice has been observed in poliomyelitis. When hepatitis appears concurrently with herpes zoster, it is possible that a zoster virus with hepatotropic properties is the cause.

Bleeding Peptic Ulcer: A Clinical Study of 511 Cases. A. Aldman and S. Wallensten. Acta med. scandinav. 155:205-222 (No. 3) 1956 (In English) [Stockholm, Sweden].

Four hundred five men and 106 women between the ages of 30 and 80 years with bleeding gastroduodenal ulcers were treated at the medical and surgical departments of Serafimerlasarettet in Stockholm, Sweden, between 1942 and 1953. Two hundred thirty of the 511 patients had mild hemorrhage and 281 severe hemorrhage. Hemoglobin and red blood cell determinations were used as criteria of the seriousness of the hemorrhage. Patients with a drop of hemoglobin to 50% or less and a red blood cell count of 2 million or less were considered as having severe hemorrhage and all the others as having a mild hemorrhage. The seriousness of the hemorrhage and the measures to be taken were determined largely by the volume and the rate of bleeding. The type of the ulcer, the age of the patient, and the duration of the condition seemed to be of less importance wtih respect to prognosis. The patient's general condition at the time of admission or at some other arbitrarily chosen time did not provide any reliable basis for assessing the prognosis.

Conservative therapy was indicated in most of the patients. There was a gradual increase in the number and the volume of blood transfusions in the course of the later years of the 10-year period. Partial gastrectomy was performed only in 22 patients whose lives were threatened by the hemorrhage despite generous blood transfusions. X-ray examination was performed immediately on admission in 57 patients with bleeding ulcers. In 41 patients it revealed a niche in the duodenum or stomach from which the hemorrhage was believed to originate. Deformation of the duodenal bulb suggested the presence of a bleeding ulcer in 10 patients. There were only six patients in whom the roentgenograms did not give any information with regard to the source of the bleeding. In 45 of the 57 patients the x-ray examination had to be performed with the patient in recumbent position; in none of them was the hemorrhage increased by the x-ray examination.

Twenty-three of the 511 patients died, a mortality rate of 4.5%. Only one of the 230 patients with slight hemorrhage died, but 22 (7.8%) of the 281 patients with severe hemorrhage died. With more abundant blood transfusions the mortality rate was reduced from 7% during the period from 1942 to 1945 to 3% during that from 1950 to 1953. The mortality rate in the patients subjected to partial gastrectomy also decreased with the introduction of modern shock therapy and improved techniques of anesthesia. In patients with massive hemorrhage the blood lost should be replaced as rapidly as possible by ample blood transfusions; if despite this measure the bleeding does not stop and the life of the patient is threatened, surgical intervention should be considered and it should be performed as soon as possible after the onset of the hemorrhage. Speedy surgical intervention is particularly advisable in patients over 60 years of age.

Pseudomembranous Enterocolitis and Antibiotics. C. R. Newman. Ann. Int. Med. 45:409-444 (Sept.) 1956 [Lancaster, Pa.]

Newman discusses pseudomembranous enterocolitis on the basis of many literature reports, and he describes the histories and autopsy studies of 12 patients with this disease observed in several small hospitals. Pseudomembranous inflammation of the intestine has been recognized for over a century, but during recent years there has been an apparent increase in its incidence. There is disagreement regarding the role of antibiotics in the production of this condition. A wide variety of causes, such as inorganic or metabolic poisons, bacterial infection, or mechanical factors, may play a part in it. Antibiotics appear to play a significant part in its development in many instances. They cannot, however, be solely responsible for all cases. Multiple factors are probably responsible, even in cases in which antibiotics have been administered. Either superinfection or the development of antibiotic-resistant organisms appears to be the greatest hazard in the use of the antibiotics. Superinfection results from a disturbance in the normal bacterial flora of the body cavities. The reciprocal inhibitory effect is therefore destroyed or lessened. Superinfection may involve the same organ of the body in which the primary infection occurred or a different one. Organisms hitherto unlikely to produce serious disease may occasionally cause a secondary infection more serious than the primary disease and may sometimes cause death. These secondary infections respond poorly to known antibiotics. They occur most frequently from two to five days after initiation of antibiotic therapy, the patient appearing to have a relapse after an initial period of improvement. Frequent cultural studies are necessary to foresee or promptly recognize a serious superinfection.

There is evidence that micrococci (staphylococci) play a major role in the development of severe pseudomembranous enterocolitis, because they are much more adaptable to antibiotics than is the normal intestinal flora. Carriers in a community or hospital where many patients have been treated with antibiotics are probably the source of these resistant organisms. The micrococcic enterotoxin very probably leads to the formation of a pseudomembrane by its direct irritant action and presumably also produces generalized systemic effects. Although erythromycin offers a great deal of help in treatment, micrococci seem gradually to become resistant to this drug also. Enterocolitis should be thought of whenever a relapse occurs during an illness, after injury, or after an operation, particularly when antibiotics have been used. If diarrhea, paralytic ileus, fever, dehydration, loss of blood volume, and collapse are present, vigorous treatment is necessary. Reports indicate a rising index of suspicion, inasmuch as more cases are being diagnosed before death, and early treatment will doubtless produce better results. Efforts should be made to prevent the enterocolitis that is related to the use of antibiotics by (1) preventing the development of organisms that are resistant to antibiotics and (2) by detecting resistant organisms before severe untoward reactions occur.

The Importance of the Fractional Serum Bilirubin Determination in Clinical Medicine. C. J. Watson. Ann. Int. Med. 45:351-368 (Sept.) 1956 [Lancaster, Pa.].

The observations of Hijmans van den Bergh on the essential difference between the prompt direct and the delayed or indirect reacting fractions of the serum bilirubin are supported by recent observations, especially those of Cole and Lathe on the polar, or water-soluble, and nonpolar, or water-insoluble, character of the two types. The hitherto undescribed bilirubin sulfate is a polar compound exhibiting a prompt direct diazo reaction. The ease with which nonpolar, crystalline bilirubin can be isolated from sources such as bile, in which the initial behavior is almost entirely polar, is more in accord with a complex than an intrinsic molecular difference. The validity of measurement of the direct reacting bilirubin at one minute deserves more emphasis. Measurement at 30 minutes includes significant fractions of the delayed, indirect, or nonpolar bilirubin. This is well demonstrated when the values at 1 and 30 minutes and the total (after alcohol), obtained with serum from patients with uncomplicated hemolytic jaundice, are compared with the amounts of polar and nonpolar bilirubin from the same samples, separated by reverse phase chromatography. The correspondence between one-minute and polar bilirubin is excellent. The 30-minute direct bilirubin, however, clearly includes nonpolar bilirubin.

During the last 10 years the fractional serum bilirubin determination, one-minute and total, has been used routinely in the University of Minnesota Hospital and the Minneapolis Veterans Hospital. The author emphasizes that the experiences accumulated during these 10 years with the determination of one-minute and total bilirubin and bilirubin ratios in relation to the clinical problems of jaundice, liver and biliary tract disease, and anemia, has fully confirmed the usefulness of this fractionation. The following points are cited as evidence that the fractionation often enhances the value of the serum bilirubin studies. 1. The one-minute bilirubin is often increased significantly within a normal value for total bilirubin. This has been observed especially in patients with early hepatitis, cirrhosis, common-duct stone, and hepatic carcinomatosis. The finding is of value in revealing an abnormality and, while not differential in itself, often points to the presence of disease of the liver or biliary tract. 2. Low bilirubin ratios in patients with elevated total serum bilirubin are indicative of retention jaundice in varying degree. The lowest ratios (<20%) are characteristic of hemolytic disease or constitutional hepatic dysfunction of the Gilbert type. The Dubin-Johnson type of jaundice and hepatic dysfunction generally exhibits ratios above 40%, most often in the range characteristic of ordinary regurgitation jaundice. 3. While the majority of patients with jaundice due to parenchymal liver disease have bilirubin ratios in the same general range as those found in cases of biliary obstruction (45 to 80%), there is a significant number of patients with diffuse liver disease in whom ratios below 40% are encountered. In the range of 35 to 40% there is small likelihood of confusion with (benign) biliary obstruction, and below 35% almost none.

SURGERY

Mitral Valvotomy: A Progress Report. R. W. D. Turner and H. R. L. Fraser. Lancet 2:525-531 (Sept. 15) and Lancet 2:587-592 (Sept. 22) 1956 [London, England].

The first 250 patients from the cardiac department of the Weston General Hospital, Edinburgh, who were subjected to mitral valvotomy were analyzed with regard to various factors that may influence the operative result. These patients were all followed for more than 12 months: 202 for more than two years, 116 for more than three years, 37 for more than four years, and 9 for more than five years. Ninety-seven per cent had either tight (finger-tip) or fairly tight (terminal phalanx) stenosis. The ages of the patients ranged from 16 to 60, and 29 were aged more than 50. Forty-four per cent had auricular fibrillation, 27% had calcification of the mitral valve, and in 19% an intracardiac clot was found at operation. Two hundred fifty other patients with mitral stenosis were seen at about the same time and not advised to have an operation, because their condition was either too mild, too severe, or complex. The electrocardiographic signs of right ventricular hypertrophy are summarized, and the value of right-side V leads is pointed out. In association with signs of uncomplicated mitral stenosis evidence of right ventricular hypertrophy invariably indicated that the stenosis was sufficiently severe to warrant operation. Some of the radiological aspects of mitral disease are discussed, and emphasis is laid on the significance of the transverse lines, which are believed to indicate distended lymphatics. Cardiac catheterization is rarely required in the assessment for operation. The operative mortality was 8%. In patients aged less than 50, even with auricular fibrillation and moderate enlargement, it was 5%. There have been only two deaths in the last 100 cases. Seven patients died from 1 to 39 months after operation.

The results were good or very good in 70% and fairly good in 10% of the patients. Analysis of the poor results revealed that systemic embolism, inadequate valvotomy, and traumatic mitral incompetence were the surgical factors concerned. The larger the heart the less likely is a good operative result to be achieved or maintained, and the least hopeful combination is a large heart with auricular fibrillation and without electrocardiographic evidence of right ventricular hypertrophy. Auricular fibrillation, enlargement, calcification of the valve, and intracardiac clot are frequent in patients over 50; consequently the operative risk is greater and the proportion of good results smaller. Nevertheless, a good result was obtained in 17 of 29 patients aged more than 50 and in 7 of 8 patients without these adverse factors. The incidence of auricular fibrillation increases with age and with heart size. The mitral valve was calcified in 27% of the patients who came to operation. Its incidence increased with age and was greater in males. Disadvantages of calcification are that effective splitting of the commissures may be impossible and attempts to achieve it increase the operative risk; good function of the valve may not be achieved despite good splitting of the commissures; and calcific embolism may take place into the systemic circulation. Despite these facts good results were obtained in more than half the patients with severe calcification. Aortic stenosis does not contraindicate mitral valvotomy for mitral stenosis, because aortic valvotomy can be carried out at the same thoracotomy. Severe cardiac cirrhosis of the liver contraindicates operation. In pregnancy operation is advised only if it is clear from the history that there was progressive dyspnea before pregnancy and that valvotomy would have been indicated in any event. Although the operative result is largely determined by the local pathological changes in the mitral valve, most patients are still being referred for operation after the optimal time has passed. Operation should be considered whenever symptoms are progressive and should be carried out unless contraindications are present.

Surgical Treatment of Cancer of the Thyroid. H. A. Kingsbury. Am. Surgeon. 22:847-856 (Sept.) 1956 [Baltimore].

Ninety-one patients with histologically proved thyroid cancer were treated at the Roosevelt Hospital in New York during the 25-year period from 1930 to 1955. Six patients could not be traced after discharge from the hospital. The remaining 85 have been followed up for periods of up to 23 years. The 91 patients were operated on by 20 different surgeons and a number of residents. The extent of operation varied with the attitude of the surgeon in charge. Among 38 patients with papillary adenocarcinoma who have been followed up for from 1 to 23 years since operation, 3 are known to have died of thyroid cancer. Two of the deaths occurred seven years after the primary operation. Of 23 patients with the diagnosis of follicular and alveolar adenocarcinoma, 4 have died. This includes three patients in whom the disease was far advanced at the time of surgery. One patient was lost to follow-up. There were two deaths among nine patients with Hürthle cell carcinoma. One patient died 13 years after the primary operation. The other had generalized metastases at the time of operation and died two months later. Among seven patients with solid adenocarcinoma, five were in an advanced stage of the disease and received palliative treatment only. Six of the seven died. Of 10 patients with giant and spindle cell carcinoma, 9 died within 18 months. One is still alive, despite numerous recurrences during the past 11 years. Sarcoma of the thyroid gland in four patients was uniformly fatal in a short time.

Vagotomy and Gastroenterostomy in the Surgical Treatment of Duodenal Ulcer. K. R. Trueman and D. L. Kippen. Canad. M. A. J. 75:547-550 (Oct. 1) 1956 [Toronto, Canada].

Twenty-five women and 80 men between the ages of 22 and 78 years with intractable or complicated duodenal ulcer underwent vagotomy and posterior gastroenterostomy at the Winnipeg Clinic in Canada, between May, 1946, and December, 1953. Symptoms had been present for an average of 12 years. Intractable pain was present in 101 patients; it was accompanied by hemorrhage in 41, perforation in 18, and pyloric obstruction in 15. Ninety-three patients were followed up for from 3 to 10 years. Control of the peptic ulcer by vagotomy and gastroenterostomy was good in 77 patients (82.8%) and fair in 6 (6.4%). Results were poor in 10 patients (10.7%). Recurrence of chronic peptic ulceration was demonstrated in only three patients. Moderate hemorrhage without symptomatic or radiological evidence of chronic peptic ulcer accounted for 3 of the 10 poor results. Although postoperative gastrointestinal disturbances of some degree occurred in 11 patients, they were considered to be undesirable side-effects of the operation in only 5. The other six patients had symptoms referable to an irritable colon, which was present before the operation.

Cancer of Stomach and Gastric Ulcer. J. de M. Grey and L. F. de Moraes. Rev. brasil. cir. 32:91-100 (July) 1956 (In Portuguese) (Rio de Janeiro).

Cancer of the stomach coexisting with gastric or duodenal ulcer is far more frequent than is believed. The ulcers are potentially cancerous. They call for surgical treatment whenever the clinical symptoms and roentgen signs persist or reappear after discontinuance of medical treatment and of diet. The period of waiting before resorting to surgery should be no more than five or six months for a duodenal ulcer and three or four months for a gastric ulcer. Three cases are reported. The first patient had resection for a simple gastric ulcer. Histopathological examination of the removed specimen showed the aspects of an ulcer with cancer developing at the base of the ulcer. The second patient had a clinical and roentgen diagnosis of antral cancer. During laparotomy for subtotal gastrectomy, enlarged lymph nodes were observed at the lesser curvature and the cardia. A total gastrectomy was performed. Histopathological examination did not reveal cancer in the antral tumor, but the lymph nodes proved to be metastases of mucoid carcinoma. The third patient, a man of 70, complained of gastric symptoms of two years' duration. Roentgen examination showed an antral tumor. During laparotomy for subtotal gastrectomy another tumor was observed. It was larger than the antral tumor and was located on the greater curvature and the cardia. Histopathological examination showed two distinct tumors of the same type, without any involved tissue between them. The authors advise early gastrectomy for gastric and duodenal ulcers that do not respond to diet and medical treatment and also for gastric tumors presenting the roentgen appearance of gastric cancer.

Clinical and Pathophysiological Problems of Total Gastrectomy in Patients with Carcinoma of the Stomach. T.-O. Lindenschmidt. Ztschr. klin. Med. 154:200-215 (No. 2) 1956 (In German) [Berlin, Germany].

Thirty-three men of the average age of 56 years and 17 women of the average age of 62 years with advanced carcinoma of the stomach were operated on at the surgical clinic of the University of Hamburg-Eppendorf, Germany, between 1950 and 1954. Forty patients had total gastrectomy and 10 had subtotal gastrectomy with 1, 2, or 3 cm. of stomach left below the cardia. There were 22 operative deaths. Fifteen patients died within from 3 to 36 months after their discharge from the hospital following the operation. Three patients were lost to follow-up. Ten patients are living with an average survival time of 30 months. The tumors invaded all the parietal layers in all the patients. Metastases were found at the operation in the lymph nodes of 6 of the 15 patients who died after their discharge from the hospital. Of the 10 still living, only one had metastases of the lymph nodes of the omentum, which was removed at the operation.

The author is convinced that indications for surgical treatment of advanced carcinoma of the stomach should be widened. There are no reliable historical, clinical, or roentgenologic data excluding operability of the tumor. Subtotal or total gastrectomy, with simultaneous removal of all the suspicious lymph nodes and of the metastasized omentum, if necessary, is required if the size of the tumor is such that the resection, either toward the pylorus or toward the cardia, cannot be made at a distance of at least 5 cm. from the tumor. The simultaneous removal of adjacent organs affected by the tumor must be decided on in the course of the intervention. Pathophysiological considerations do not limit subtotal or total gastrectomy, provided that the patient is given adequate substitution therapy in the preoperative and postoperative period. Such therapy should consist of adequate administration of proteins in order to break through the vicious circle between protein deficiency and enzyme deficiency. Pancreas preparations should be supplied to improve the utilization of proteins and fats. Parenteral iron therapy is indicated in the presence of anemia due to iron deficiency. Vitamin B_{12} and folic acid therapy are indicated in the presence of megaloblastic anemia. Vitamin B complex therapy is important for the prevention or treatment of manifestations of vitamin B deficiency after total gastrectomy, such as glossitis, pharyngitis, cheilitis, and esophagitis. Total gastrectomy is not indicated in patients in whom all the adjacent organs, i.e., liver, pancreas, spleen, diaphragm, mesocolon, and colon, have become infiltrated by the carcinoma, requiring such a formidable intervention that only exceptional patients may survive. In addition, the prognosis is not favorable as regards freedom from relapses and metastases in patients with involvement of suprapancreatic and para-aortal lymph nodes. and it is particularly unfavorable in patients in whom the tumor has invaded all of the parietal layers.

Primary Resection of Stomach in Free Perforation of Gastroduodenal Ulcers. R. Baltzersen. Nord. med. 56:1195-1196 (Aug. 23) 1956 (In Norwegian) [Stockholm, Sweden].

In Haukeland Hospital in Bergen 179 cases of free perforation of gastroduodenal ulcers (134 cases of perforated duodenal ulcer, 45 of perforated gastric ulcer) were treated from 1942 to April, 1955, with a total mortality of 9.5%. Primary resection of the stomach according to Billroth 2 or its modifications was done in 118 of the cases, with 5 deaths, all in men with duodenal ulcers. From 1938 to April, 1955, a total of 313 gastroduodenal perforations into the free peritoneal cavity were treated with 32 deaths or a mortalityy of 10.2% Of the 175 patients in whom primary gastric resection was performed, 7, or 4%, died; they were all treated for perforated duodenal ulcer. Only one death occurred in the 67 primary resections performed after 1947, giving an operative mortality of 1.5%. In the 605 gastric resections performed in the same period for nonperforating ulcers the mortality was 1.2%.

Experiences with the Treatment of Acutely Massively Bleeding Peptic Ulcer by Blood Replacement and Gastric Resection. J. D. Stewart, J. H. Cosgriff and J. G. Gray. Surg. Gynec. & Obst. 103: 409-415 (Oct.) 1956 [Chicago].

Immediate blood replacement and early gastric resection has been used by Stewart and associates since January, 1947, in the treatment of patients with massively bleeding peptic ulcer. They review observations on 193 patients on whom 196 operations were performed. Chronic duodenal ulcer, penetrating in nature, was the commonest lesion, while chronic gastric ulcer was second in frequency. Shallow ulcer associated with a brief or nondescript history of ulcer dyspepsia was not uncommon, accounting for approximately 20% of the gastric lesions. In 21 patients the site of bleeding was not satisfactorily determined at operation. During the series of 196 operations on 193 patients, 22 patients were found to have other causes for bleeding. There were 13 malignant lesions of the stomach and 4 of the duodenum and pancreas. Of the 3 patients with hemorrhage from esophageal varices, one had extrahepatic portal bed block, or Banti's syndrome. The appropriate operation was carried out when the true diagnosis became evident in these 22 patients, and at least one of those who had gastric resection for hemorrhagic gastric carcinoma under these circumstances is alive and well over five years later. Subtotal gastrectomy was performed in 186 of the patients.

Twenty-five of the patients died. There were two deaths among the 65 patients less than 50 years old (3%) and 23 (18%) among the 128 patients over 50 years of age. Half of the patients who recovered and three-quarters of those who died had serious associated diseases. There was a high incidence of cardiovascular disease in patients over 50 years of age. The commonest postoperative complications in patients who recovered were wound infection and dehiscence, pulmonary atelectasis, and pneumonia; commonest in those dying were cardiac complications. Dehiscence of the duodenal stump, stomal arrest, transfusion reaction, and postoperative hemorrhage were rare. The average amount of blood given before and during operation was 2,600 cc.

The Management of Ascites with Radioactive Gold. R. J. Ireton and J. C. Ullery. Surg. Gynec. & Obst. 103:437-442 (Oct.) 1956 [Chicago].

Radioactive colloidal gold (Au^{198}) has been used in the treatment of ascites at the Ohio University Hospital since 1952. The group treated included 35 patients with proved ascites secondary to tumor. Three of these patients received a second Au^{198} treatment, for a total of 38 treatments. There were 3 men and 32 women with an average age of 55 years, the youngest 29 and the oldest 75 years old. The type of tumor varied, but the majority were some type of adenocarcinoma. Two-thirds of the adenocarcinomas were primary in the ovary. The patients were divided into 3 groups. Group 1 is composed of patients with no evidence of reaccumulation of ascites at the time of follow-up or death. There were nine patients in this group, five of whom are still living after from 2.5 to 17 months. Group 2 consists of patients who had a remission of ascites for at least six weeks. There were seven patients in this group, four of whom are still living after from two to six months. Group 3 consists of those patients in whom there was no remission or only transient remission of ascites. There were 19 patients in this group. Nine of these patients expired within six weeks of treatment and only two are still living, for five and nine months respectively.

Factors that might explain the differences in the results are reviewed, with the following conclusions: 1. The type of tumor was of some importance, since none of the patients with sarcomas had remissions. 2. That the smaller metastasis was associated with better results was only indicated, not proved. 3. Treatment prior to Au^{198} therapy, treatment after Au^{198} therapy, or combination of the two, whether surgery, radiation, or both, was of little significance in the remission of ascites. 4. The general condition of the patient was important, since one-half of the patients experiencing no remission died soon after treatment. One-half of the patients with pain obtained relief. Complications solely attributable to Au^{198} were uncommon and minor. The authors make a plea for the earlier use of Au^{198}, suggesting that it should be used prophylactically.

A Clinicopathologic Study of the Epiploic Appendages. T. E. Lynn and J. M. Waugh. Surg. Gynec. & Obst. 103:423-433 (Oct.) 1956 [Chicago].

This inquiry into the conditions produced by disease of the epiploic appendages is based on literature reports and on a detailed review of the clinical, surgical, and pathological data in 17 patients observed at the Mayo Clinic from 1940 to 1953. The available literature revealed reports of 156 cases of symptomatic pathological changes of the epiploic appendages prompting surgical intervention. Inflammation (appendagitis) was present in 109 of these cases, intestinal obstruction had been produced by the appendage in 13, and in 34 the appendages were intrahernial. There was primary intra-abdominal appendageal disease in 12 of the 17 patients treated at the Mayo Clinic and in two of these the presenting picture was that of intestinal obstruction. Intrahernial epiploic appendagitis occurred once. In the remaining four patients, other disease processes caused the major symptoms or incited the pathological changes in the appendages. During the same period 129 instances of diseased epiploic appendages without symptoms were found; the majority of these appendages had become detached and were found as intraperitoneal loose bodies.

Pathological changes in epiploic appendages may mimic many acute abdominal inflammatory syndromes; they may form an intra-abdominal mass or produce mechanical intestinal obstruction. They may also be a source of pain in a hernia or may be the sole occupant of an incarcerated hernia. Detached epiploic appendages are the most frequent cause of intraperitoneal loose bodies. These may become secondarily attached elsewhere in the abdomen and be confused with a neoplastic process. Infarction of epiploic tags with superimposed epiploic appendagitis has usually been confused clinically with acute vermiform appendicitis. A preoperative distinction can only be tentative. Should laparotomy fail to disclose the usual sources of acute abdominal pain, epiploic appendagitis deserves consideration. An inflamed epiploic appendage may occasionally produce chronic or recurrent symptoms. The treatment is surgical excision of the diseased appendage. Rarely, a diverticulum of the colon will be encountered within the appendage.

Problem of Intrahepatic Cholangitis Accompanying Cholelithiasis. T. Burckhart. Chirurg 27:408-412 (Sept.) 1956 (In German) [Berlin, Germany].

Eighty-six women and 26 men, 68 of whom were between the ages of 41 and 60 years, underwent cholecystectomy at the surgical clinic of the University of Mainz, Germany, because of a definite clinical suggestion of lithiasis. A preoperative diagnosis of cholangitis had not been made in any of the 112 patients. Biliary calculi were present in the gallbladder in 102 patients and in the common bile duct in 10. Chronic cholecystitis was observed in 93 patients, and only 5 were without abnormal changes in the wall of the gallbladder. A biopsy specimen was obtained from the liver in all patients in the course of the cholecystectomy. Intrahepatic cholangitis was found in 37 patients; other changes in the liver, including pronounced lymphocyte infiltration of Glisson's capsule, increased interstitial connective tissue, diffuse or central fatty degeneration, biliary cirrhosis, and brown atrophy, were present in 36 patients. Fifty-one patients had a history of icterus or were jaundiced at the time of the operation. Nine of the 11 patients between the ages of 61 and 76 years had abnormal changes in the liver, but none of the 33 patients between the ages of 17 and 40 years had such changes. The incidence of cholangitis increases with advancing age. The duration of the cholelithiasis was less than one year in 49 patients, 35 of whom had cholangitis. One-half of the patients with cholangitis also had icterus.

These findings suggest that the presence of a clinically more or less silent intrahepatic cholangitis must be considered as an accompanying disease in patients with apparently uncomplicated cholelithiasis and cholecystitis. Appropriate preoperative treatment should be instituted. Removal of a small biopsy specimen, which in the author's patients was performed without any damage or complication, is justified. The incidence of residual or postoperative complaints after cholecystectomy will thus be reduced and severe early and late complications prevented.

Outcome of Surgery for Ulcerative Colitis. B. N. Brooke. Lancet 2:532-536 (Sept. 15) 1956 [London, England].

What is the expectation of life of patients who have had total colectomy for ulcerative colitis? To find an answer to this question Brooke reviewed the records of the 131 patients with ulcerative colitis who had been operated on by him. In five patients only emergency or diagnostic laparotomy was undertaken; 126 underwent elective surgery (117 excision and permanent ileostomy and 9 resection and anastomosis). The group included 84 females and 47 males. The youngest patient operated on was 6 years old, the colitis having started two years earlier. Operation was resorted to when the patient's general condition had continued to deteriorate despite conservative measures; when the patient was otherwise unlikely to return to normal life; for complications, both anorectal and remote, for the acute emergencies of hemorrhage and perforation, for carcinoma; or to remove this potential hazard in late cases.

There were 15 operative and late deaths. This represents a mortality of 12%—about half the mortality of the disease treated conservatively in the precortisone era. The majority of late complications of operation arose in connection with the ileostomy. Eversion suture of the mucosa to the skin is advocated to reduce the incidence of stenosis. Revision of the ileostomy was required in some cases to enable the patient to use an adherent ileostomy bag. A follow-up extending to five years and longer in over a third of the survivors indicates that ileostomy should no longer be dreaded as an impediment to full, normal life; indeed, it restores patients with ulcerative colitis to full work, full weight, and an enjoyment of ordinary pastimes. In about half the patients the diet has to be restricted slightly. Patients regard their ileostomies as satisfactory. Resection and anastomosis with preservation of the anal sphincter (9 cases) has been less satisfactory in this series than excision and permanent ileostomy (117 cases). The disease may recur after sphincter-saving resection, and its complications may then arise for the first time This method is not recommended as a routine, and its indications are limited; it is precluded for rectal hemorrhage and perforation.

Inguinal Hernia in Female Infants and Children. C. T. Kristiansen and W. H. Snyder Jr. West. J. Surg. 64:481-484 (Sept.) 1956 [Portland, Ore.].

Incarcerations in inguinal hernias are frequent in both male and female infants and frequently require emergency surgery. Kristiansen and Snyder of the California Children's Hospital made a study of incarcerations in the female infants who had received treatment at their hospital from January, 1946, through January, 1955. Of a total of 3,142 inguinal hernias, 351 occurred in girls. One hundred four of the 2,791 hernias in boys were incarcerated or strangulated (3.7%), whereas 51 (15%) of the 351 inguinal hernias in girls were incarcerated or strangulated One hundred sixty or 45% of the hernias in female infants occurred in the group aged one year or under, and this age group contained all of the incarcerated hernias in female infants and children. After the first year of life the incidence of hernias is fairly constant for each year, with no incarcerations or strangulations. Ovary only, ovary and tube, or ovary and small intestine were found in the hernial sac of all but 3 of the 51 female infants with incarcerated inguinal hernia. The ovary and tube were swollen with some discoloration in almost every instance, indicating that prolonged delay may result in some permanent damage to the ovary and its follicles. Tissue death was observed in only one of the infants and even here the ovary was not removed The authors believe that the surgeon can rely on the recuperative powers of the ovary. The organ should not be removed, but should be replaced in the abdomen. Infants and children tolerate surgical repair of a hernia very well, and since there is a negligible mortality, surgical treatment should be carried out as soon as a hernia is discovered. In view of the fact also that the incidence of incarceration is highest in the first year of life, the age of the infant should be no deterrent to operative intervention. This is especially true in female infants, as in this study incarceration occurred five times as frequently in the females as in the males

Giant Cell Tumor of Tendon Sheath. F. L. Flack. J. Oklahoma M. A. 49: 339-340 (Sept.) 1956 [Oklahoma City].

The patient was a 48-year-old woman who had had some pain and swelling of her hand for 10 years but who had continued her employment as a maid in a hotel until shortly before admission to the hospital, when she caught her hand in a clothes wringer This forced her to seek help because of greatly increased pain

There was a tumor mass measuring 20 by 15 cm. involving the entire left hand. The fingers seemed to stick out of the mass. There were many ulcerations, some of them 3 to 4 cm. in diameter. The whole mass was hot, red, tender, and foul smelling. An x-ray film of the hand showed erosions of the cortices of the metacarpals and phalanges with dislocations of some of the joints. Two days after admission she was given 500 ml. of whole blood, but a day later her hematocrit was only 16. She received 500 ml. of whole blood daily for the next five days, and on the ninth hospital day, the patient having received 7 million units of penicillin over this period, the arm was amputated just above the elbow. She was ambulant the next day and was discharged from the hospital on the 12th postoperative day with all of the incisions well healed.

The tumor on microscopic examination proved to be a giant-cell tumor of the tendon sheath. In some sections there were multiple nodules with many foam cells. In others there were nodules composed of giant cells. All through this nodular tumor were acute and chronic inflammatory cellular elements. The foam cells seem to be of special significance, since they are rarely seen in malignant tumors thought to arise from periarticular structures but are a characteristic feature of the benign lesions arising in the same structures. A giant-cell tumor of a tendon sheath reaching a size like that of the tumor described is a very rare finding.

Pathological Fractures: Treatment by Internal Fixation and Irradiation. M. B. Devas, J. W. Dickson and A. M. Jelliffe. Lancet 2:484-487 (Sept. 8) 1956 [London, England].

The results of internal fixation in a series of 18 pathological fractures are described. The operation should be done early, since any delay will increase the difficulty of resetting the displaced fragments. Postoperative swelling is the rule, but pain is not severe and can be controlled by analgesics. The method of internal fixation will vary with the site of the fracture. In the present series, seven malignant and one nonmalignant pathological fracture of the shaft of the femur have been stabilized with a Küntscher nail. Six fractures due to metastases and one due to a nonmalignant lesion of the femoral neck and intertrochanteric region have been stabilized with a Smith-Petersen pin or with a nail and plate. Three pathological fractures of the shaft of the humerus due to metastasis have been treated by the insertion of a Rush pin.

The techniques for the internal fixation of pathological fractures are identical with those for the internal fixation of nonpathological fractures, and the same attention must be paid to gentle handling of the tissues, accurate placing of the chosen device, and absolute asepsis. An antibiotic cover is advisable if there is any doubt as to the complete sterility of the procedure. Closed reduction of the fracture is the safest method, but open reduction may be needed because of malignant infiltration at the fracture site. The results of internal fixation in this small series have been satisfactory. All patients experienced considerable or complete relief of pain, and some patients with widespread malignant disease were able to resume an active life. Postoperative pain was easily controlled, and no patient died as a result of the procedure. The authors believe that all pathological fractures of the long bones should be considered for operation. Prophylactic internal fixation is indicated where there is a real risk of fracture.

NEUROLOGY & PSYCHIATRY

Penicillin Treatment of Asymptomatic Central Nervous System Syphilis: I. Probability of Progression to Symptomatic Neurosyphilis. R. D. Hahn, J. C. Cutler, A. C. Curtis and others. A. M. A. Arch. Dermat. 74:355-366 (Oct.) 1956 [Chicago].

Of a total of 765 patients with asymptomatic syphilis of the central nervous system who were treated with penicillin at eight different hospitals, 34 (4.4%) were given less than 2,400,000 units as the total dose of the antibiotic, 163 (21.3%) were given total doses of penicillin varying between 2,400,000 and 4,799,999 units, 258 (33.7%) were given total doses varying from 4,800,000 to 8,999,999 units, 306 (40%) were given 9 million units or more, and in 4 (0.5%) the amount of drug given was unknown. Two hundred sixty-four patients had not received previous treatment, and whatever previous treatment the other 501 patients had been given was inadequate to produce a cure. The 765 patients were followed up after the penicillin treatment for periods ranging up to six or seven years. The maximum cumulative probability of clinical progression from asymptomatic to symptomatic neurosyphilis was calculated in these patients as 0.55% at the first year, 1.69% at the third year, 2.02% at the fifth year, and 3.31% at the seventh year after the treatment for syphilis. Only 12 of 765 treated patients were recorded as having shown progression of asymptomatic neurosyphilis at the last observation period. Of these patients, only one was unequivocally a treatment failure; this patient responded satisfactorily to retreatment with a larger dose of penicillin. In the other patients there was no clear-cut evidence that the so-called progression did in fact represent progress of the disease process.

In this group, progression could not be related to any of the factors, such as age, race, sex, previous treatment, and retreatment status, considered in the analysis, except in a single patient in whom lack of cooperation precluded treatment when spinal fluid examination clearly indicated a relapse requiring retreatment. Progression, with but one exception, consisted of what can be considered minor neurological or psychiatric changes, and none of the patients was incapacitated by the so-called progression. It is probable that what is considered as progression represents manifestation at the level of clinical recognition of pre-existing subclinical neuraxis damage. The authors' observations suggest that asymptomatic syphilis of the central nervous system responds extremely well to treatment with penicillin; within the study period of from six to seven years it appears that penicillin alone is capable of completely curing asymptomatic syphilis of the central nervous system.

Penicillin Treatment of Asymptomatic Central Nervous System Syphilis: II. Results of Therapy as Measured by Laboratory Findings. R. D. Hahn, J. C. Cutler, A. C. Curtis and others. A. M. A. Arch. Dermat. 74:367-377 (Oct.) 1956 [Chicago].

This report deals with the pretreatment and post-treatment status in terms of results of blood and spinal fluid examinations of the 765 patients with asymptomatic syphilis of the central nervous system who were treated with penicillin and were evaluated in the preceding paper with regard to the probability of progression to symptomatic syphilis. Changes in results of laboratory tests after treatment with penicillin were related to the test status of the given patient in a given clinic at the time of the study treatment with penicillin. Test results were considered to be essentially unchanged, less positive, or more positive. In this way changes in laboratory findings from the eight hospitals in which the patients were treated were analyzed as in a single group of patients. The range of cell count in the cerebrospinal fluid of from 5 to 10 and total protein of from 40 to 50 mg. per 100 cc. was to be considered a borderline zone and was probably within the limits of normality. After successful treatment with penicillin, abnormal cell counts disappeared almost completely within four years; total protein values changed more slowly and did not show the same degree of reversion to what were considered normal limits within that period.

As measured by the fall in cell count, which is the most sensitive index, no clear-cut relationship between success or failure of treatment and size of penicillin dosage could be demonstrated. At most, from cell count studies, it would seem that 9% of the patients might be expected to show a need for retreatment at the end of one year's observation, without regard to the original penicillin dose used. This probably represents a composite group of patients who are failures and patients slow to respond.

It appears that persistently abnormal spinal fluid total protein levels are not, in themselves, indicative of poor prognosis. Significant differences in total protein response were observed in relation to sex and race. The total protein outcome was less favorable in white persons than in Negroes and in men than in women. Spinal fluid tests for syphilis showed a gradual decrease in positivity with the passage of time after treatment; this was more pronounced in the group receiving only a single course of penicillin. Improvement in the spinal fluid test for syphilis was more rapid in the younger patients, in those with disease of shorter duration, and in those with abnormal cell count. A minimum of 28% of the patients with asymptomatic neurosyphilis had a blood serologic titer of 2 units or less. Thus, a weak serologic reaction cannot be considered as indicating absence of spinal fluid involvement. After penicillin treatment of asymptomatic syphilis of the central nervous system there was a gradual trend toward seroreversal, with some patients having more strongly postive results from the serologic test or having positive results after previous negativity. There seemed to be no relationship between serologic negativity and degree of spinal fluid positivity at the onset of the study treatment with penicillin. Changes in the blood serologic test for syphilis after penicillin treatment did not reflect, with any degree of accuracy, changes in the spinal fluid test for syphilis.

Asymptomatic syphilis of the central nervous system responded extremely well to treatment with penicillin. Retreatment on the basis of persistent positive laboratory findings alone is not recommended unless the cell count increases significantly after treatment, remains unchanged at an elevated level for six months after treatment, or increases significantly after approaching normalcy or near-normalcy after treatment.

GYNECOLOGY & OBSTETRICS

Variables in the Diagnosis and Management of Vulvar Carcinoma as Observed by the Philadelphia Committee for the Study of Pelvic Cancer. G. A. Hahn. Am. J. Obst. & Gynec. 72: 756-770 (Oct.) 1956 [St. Louis].

The 131 women with vulvar carcinoma reviewed were treated in 20 different Philadelphia hospitals. The patients were almost equally divided between parous and nulliparous women. Ninety-nine of the women had ceased having menstrual periods, the menopause having been artificial in 11 of them. The most common symptoms causing the patient to seek medical advice were, in the order of their frequency, pruritus, a lump, bleeding, dysuria, pain, ulcer, and discharge. Diabetes mellitus existed in eight of the patients, and six had primary carcinoma elsewhere: two in the breast, one in the buttock, and three in the genital organs (endometrium, ovary, and cervix). The breast and cervical cancers had been diagnosed before, and the carcinomas of the buttock, ovary, and endometrium were discovered at the time the vulvar lesion was being studied.

Delay on the part of the patient alone was a contributing factor in the failure to obtain adequate treatment in 45 instances. In 42 additional patients, physicians or institutions or both had caused further delay, that is, "patient delay" was a factor in 87 (66.41%) of the women. The average delay in seeking a physician's advice was 2.35 years and the longest delay was 12 years. Hope that the difficulties would disappear with time, fear of cancer or that some surgical procedure might be necessary, being too busy, absence of pain, or being too old for any type of surgery were reasons given for not consulting a physician. Only once was finances given as the reason for not asking for a physician's help.

There were 24 women (18.31%) in whom physicians were considered to be wholly to blame for delaying the diagnosis of vulvar malignancy. Three times an institution was considered to be at fault, and in five cases an institution was considered to have contributed to delay. More than one physician was responsible for delay in 12 instances. One patient had visited five physicians before an adequate diagnosis was made. One patient had been hospitalized in two different institutions for orthopedic treatment and had also been under the care of a private physician. The final step in her diagnosis was made by a registered nurse who noted the vulvar growth during her care of the hospitalized patient. In most cases failure to examine the patient was the cause for the delay in making a proper diagnosis. Improper diagnosis was the next most common cause of physician delay. Sixteen different types of treatment, or treatment combinations, were employed in the 127 patients who were treated. Radical vulvectomy with node dissection was most frequently used, then radical vulvectomy alone, and finally x-ray therapy. Fifty-seven patients observed five or more years had a survival rate of 47.37%. The patients who had been treated by radical vulvectomy and bilateral groin dissection had a five-year survival rate of 78.94%. The author believes that the most important factor bringing about a favorable five-year survival rate is the type of therapy rather than the delay involved.

Value and Risk of Pertubal Insufflation. P. Lange. Acta Obst. et gynec. scandinav. 35: 354-365 (No. 3) 1956 (In English) [Stockholm, Sweden].

Two hundred ninety-one women were subjected to 342 kymographic uterotubal insufflations at the fertility department of the Municipal Hospital of Copenhagen, Denmark, between Jan. 31, 1951, and Dec. 31, 1952. Uterotubal insufflation revealed tubal nonpatency in 110 of the 291 patients. Hysterosalpingography was performed after several weeks or months in 83 of the 110 patients. Tubal nonpatency was confirmed by hysterosalpingography in 46 of the 83 patients. Hysterosalpingography showed a normal tubal picture in 23 patients, i.e., there was definite disagreement between the results of tubal insufflation and hysterosalpingography. Hysterosalpingography showed definite abnormal changes in the remaining 14 patients, but there was evidence of peritoneal spill suggesting a certain degree of patency. "Relative" disagreement between the results of tubal insufflation and hysterosalpingography was suggested in these patients. Thus complete agreement between the results of the two methods was found in 55.4% of the patients, definite disagreement in 27.7%, and relative disagreement in 16.9%.

Tubal patency was revealed by the first or subsequent enterotubal insufflation in 181 patients. One hundred eleven of these patients presented a normal kymographic curve; hysterosalpingography was performed in 38 of these 111 patients, and the results were normal in 30. The remaining 70 patients had an abnormal kymographic curve; hysterosalpingography was performed in 33 of these and revealed unquestionable nonpatency in 6 and various forms of anatomic abnormality in 27. The incidence of complications of uterotubal insufflation was surprisingly high with definite pelvic inflammations occurring in 11 patients, i.e., in 3% of the 342 insufflations. No death resulted from uterotubal insufflation, and only two of the 11 patients required admission to hospital, the other 9 being treated as outpatients. None of them required surgical treatment.

The therapeutic effect of uterotubal insufflation was small in that 22 of the 291 patients conceived and only 4 of these fulfilled all the criteria relating the conception to the uterotubal insufflation. The author's observations suggest that a normal kymographic tracing gives considerable certainty of tubal patency. Yet in about 5% of the patients with a normal kymographic curve hysterosalpingography revealed nonpatency. When nonpatency is ascertained by uterotubal insufflation, the examination should be repeated or hysterosalpingography performed.

A Consideration of the Problems of Radiosensitivity in Cancer of the Cervix. S. B. Gusberg. Am. J. Obst. & Gynec. 72: 804-819 (Oct.) 1956 [St. Louis].

Gusberg outlines the three principal methods for radiosensitivity testing of cervical cancer that have been used in recent years to supplement clinical analysis: histological and cytochemical methods have been used to measure the tumor response, and cytological methods have been used to measure the host response. The histological changes have been codified by Glucksmann, who claims that tumors of high differentiation are more radiocurable than those that are anaplastic. Radiosensitivity and radiocurability may not be identical concepts. The second type of investigation is cytological and concerned with host response. The thesis was developed that the radiation response of normal vaginal cells was more important than the response of tumor cells. Recent work is concerned with material obtained before treatment and with sensitization response. It is believed that, if a patient with a cervical cancer has in her vaginal smear 10% or more of benign vaginal cells with a certain quality, she will respond favorably to radiation, whereas if she has less than 10% she will respond poorly to radiation but will have an excellent result if treated surgically. Sensitization response supposedly measures an immune response by the host.

The third type of radiosensitivity investigation is that current in the author's own laboratory. It rests on the thesis that cancer cells dying under radiation will have an alteration in their nucleic acid pattern. Cytochemists have demonstrated that there are two general types of tumor cells, so-called A cells, which are viable and aggressive and have a heavy chromatin pattern (an important site of desoxyribonucleic acid [DNA]) and relatively obscure nucleoli; and B cells, which are relatively inactive, devitalized, perhaps prenecrotic tumor cells whose chromatin pattern is becoming more obscure and therefore have a relatively lowered nuclear content of DNA but whose nucleoli are very prominent, and thus have a relatively higher ribonucleic acid (RNA) configuration in their nuclei. Studies were begun on the basis of the thesis that the growing edge of a cervical cancer prior to radiation should be rich in A cells, and that this zone might show a conversion to a predominance of B cells under radiation if it were responding properly by healing. Four quadrant biopsies were obtained from the growing active zone of the tumor before, and at weekly intervals during, radiation. It was found that healing of cervical cancer in the human can be predicted with some uniformity from the observation of nuclear changes occurring within three weeks after the beginning of radiation in the growing, vital zone of the tumor. The observed changes include: (1) enlargement of the cell and its nucleus; (2) a relative diminution in DNA evidenced by a sort of dilution of the chromatin masses; and (3) a relative increase in DNA as evidenced by an increase in nucleolar size and number. It has been possible to predict tumor healing if there is a shift away from a predominance of an A cell, or active phase, in the growing zone, toward a B cell, or regressive phase. This change implies an alteration in the DNA/RNA ratio with a relative shift toward RNA predominance. The methods as yet are not precise, and these changes are relative: the RNA seems to increase at about the same rate as does the general cell and nuclear volume; the DNA, on the other hand, probably changes very little and therefore shows a relative decrease in concentration. This suggests a specific effect of irradiation on the synthesis of DNA. The author hopes that studies of nucleoprotein patterns will make it possible to predict tumor-cell death in a uniform fashion before conventional histological or clinical methods can detect it. Such cytochemical prognostication could indicate continuation of radiation for those with good response, supplementary lymph node dissection for those with fair response, and discontinuation of radiation in favor of radical hysterectomy for those with poor response.

Subarachnoid Hemorrhage and Pregnancy. D. E. Cannell and E. H. Botterell. Am. J. Obst. & Gynec. 72: 844-855 (Oct.) 1956 [St. Louis].

The authors report 16 women in whom subarachnoid hemorrhage occurred during pregnancy and who were admitted to the obstetric and neurosurgical services of the Toronto General Hospital from Jan. 1, 1950, to Dec. 31, 1955. In four patients subarachnoid hemorrhage occurred with other complications of pregnancy; three of them died. Of the two patients with preeclampsia, one died after cesarean section and the other recovered. The third patient died as a result of thrombosis of the superior sagittal sinus 32 days after an apparently normal pregnancy and delivery. The fourth patient died of subarachnoid hemorrhage from a mycotic aneurysm of the basilar artery following subacute bacterial endocarditis and septicemia after a septic abortion. The remaining 12 patients experienced subarachnoid hemorrhage in otherwise normal pregnancies. Twenty episodes or recurrences of subarachnoid hemorrhage occurred in these 12 patients. Thirteen were primary, and 7 were recurrences shortly after the initial hemorrhage. One patient had subarachnoid hemorrhage in two different pregnancies. Of 13 major primary subarachnoid hemorrhages. seven occurred in the first 20 weeks of pregnancy, four in the latter 20 weeks, and two in the puerperium. None occurred during labor, though the effects of labor as a precipitating factor cannot be discounted in the two that occurred early in the postpartum period. Six of the subarachnoid hemorrhages arose from intracranial aneurysms, three from arteriovenous malformations, and in three the source of bleeding was undetermined. Subsequent angiograms or autopsies show that aneurysms are the cause of a significant number of the subarachnoid hemorrhages said to be of "undetermined origin."

Regarding the diagnosis the authors say that severe headache, often occipital in distribution, nuchal rigidity, nausea and vomiting, loss of consciousness, hemiplegia, and involvement of cranial nerves occurred in this order of frequency. Auscultation of the skull, and particularly the eyeballs, may demonstrate a bruit, diagnostic of arteriovenous malformation. The clinical diagnosis was confirmed by the withdrawal of grossly bloody spinal fluid under pressure. Clinical neurological examination, alone, frequently fails to localize the site of the bleeding. Cerebral angiography is an indispensable step in the diagnosis. Prompt surgical treatment is indicated in pregnant patients in whom subarachnoid hemorrhage occurs as the result of a ruptured berry aneurysm or arteriovenous malformation. The obstetric management of such patients should be based upon sound obstetric principles, cesarean section being employed on indication rather than election.

ACTH and Hyperemesis Gravidarum. E. Ferrario. Minerva ginec. 8: 586-590 (July 31) 1956 (In Italian) [Turin, Italy].

The author studied the effect of corticotropin on the urinary excretion of corticoids and 17-ketosteroids in normal pregnant women and pregnant women with hyperemesis. Four patients affected with severe forms of hyperemesis were given corticotropin. Previous treatments had had no effect on these patients. The results obtained with corticotropin were very good. They seem to prove that adrenal hypofunction of adrenocortical and hypophysial origin is involved in the hyperemesis gravidarum syndrome. The dosage and administration of the hormone cannot be standardized. In general, when the administration of ACTH is stopped the symptoms reappear and readministration of ACTH is required. The authors had no side-effects with the product that they used. If the dosage is not high, the danger to the fetus is limited. Undesirable effects of the drug are dependent on the species of the animal, the dosage, and the stage of pregnancy in which corticotropin treatment is started. A very low dosage does not involve any risk. ACTH does not seem to pass the placental barrier. The possible damage to the adrenal glands of the fetus seems to be caused by the transplacental passage of excessive corticoids produced by the mother. Hyperemesis gravidarum runs its course in three well-differentiated stages: a psychogenic stage, an intermediate stage, and a stage characterized by a true gravidic toxicosis brought about by changes in metabolism caused by liver damage. ACTH would be of no help in the third stage.

PEDIATRICS

Electrolyte Considerations in Exchange Transfusions for Erythroblastosis Fetalis. R. P. Bolande, H. S. Traisman and H. F. Philipsborn Jr. J. Pediat. 49:401-406 (Oct.) 1956 [St. Louis].

The serum electrolytes were studied in 23 erythroblastotic infants before and after 26 exchange transfusions. Refrigerated blood used to replace the circulating blood of erythroblastotic infants is in many instances hyperkalemic and commonly hypocalcemic (citration effect). Under such circumstances striking alterations in the serum electrolytes of the transfused infants must be anticipated. Particular attention was paid to potassium. Many of the infants received donor blood that was markedly hyperkalemic. The majority of infants tolerated an abnormal load of infused potassium without untoward physiological effects or significant change in their serum potassium concentrations. In some instances, rapid infusion of hyperkalemic donor blood appeared to be related to cardiac arrest, death, or both. Critical values could not be definitely established from the limited data at hand. Since it is known that the potassium concentration of donor blood is progressively increased during cold storage, the safest procedures would be to use fresh, warm donor blood at a tolerable rate.

Treatment of Erythroblastosis Fetalis with Special Reference to Sensitization to Rh-Hr Factors Other than Rh_0. A. S. Wiener, I. B. Wexler and G. J. Brancato. J. Pediat. 49:381-393 (Oct.) 1956 [St. Louis].

A number of modifications in the exchange transfusion technique have been introduced by Wiener and associates. To date, 166 babies with erythroblastosis fetalis caused by Rh_0 sensitization have been treated by their latest modification of exchange transfusion by the radial artery-saphenous vein technique. In this latest modification, partially concentrated blood (hematocrit 0.5), preferably not more than three days old, is used. This is prepared by removing part of the citrated plasma after sedimentation has occurred. Depending on the severity of the disease and the size of the baby, from 450 to 900 ml. of such concentrated blood is used for the transfusion. In severe cases the exchange transfusion is repeated, but in no instance are more than two exchange transfusions deemed necessary. Among the 166 babies treated this way, only five died or had neurological sequelae, a crude mortality rate of only 3 ± 0.9%. On the other hand, among babies treated by earlier modifications, by only simple transfusion, or receiving no treatment at all, the mortality rate ranged from 17 to 21%. The difference in results is even more striking when the severity of the disease is taken into account. Thus, among severely affected babies who received no treatment the mortality rate was 65.5 ± 10.6%; among those receiving simple transfusion therapy the mortality rate was 42.1 ± 7.8%; among those treated by previous methods of exchange transfusion the mortality rate was 19.8 ± 2.6%; while among those treated by the latest modification of exchange transfusion, the mortality rate was only 3.8 ± 1%.

Erythroblastosis fetalis caused by sensitization to Rh-Hr factors other than Rh_0 poses an important problem, since the routine antenatal screening test for Rh_0 sensitization does not take them into account. Such cases are rare, but they are just as serious as instances of Rh_0 sensitization. Thus, among nine cases of erythroblastosis fetalis caused by hr′ sensitization, one baby died before treatment could be instituted. Of the remainder, four were treated by exchange transfusion and recovered, while among the four treated by simple transfusion one died and one of the three who survived had severe neurological sequelae. A simple screening test for Rh_0 antibodies consists in testing the patient's serum against ficin-treated cells of types Rh_1Rh_1, Rh_2, and rh respectively. This test should be carried out on all women in labor admitted to the obstetric service and on patients admitted to the surgical or other services who might require blood transfusion. Case histories are presented that illustrate the value of this screening test. In patients with hr′ sensitization the antibodies, even when present in high titer, may react only in tests against enzyme-treated cells and may fail to react in the conglutination and antiglobulin tests. This accounts for puzzling, severe cases of erythroblastosis fetalis in which the direct antiglobulin test for coating of the baby's red blood cells by Rh-Hr antibodies is negative. Certain antibodies, such as anti-F and anti-J, are not detected by the enzyme test, so that the screening test against ficin-treated cells should supplement and not replace the other tests for isosensitization.

Causes of Mongolism. J. Øster. Dan. med. bull. 3:158-164 (Aug.) 1956 (In English) [Copenhagen, Denmark].

An average incidence of mongolism of 1 mongol to approximately every 600 live births, or 0.17%, is reported. In Øster's studies of the cases from the lying-in departments of the Rigshospital from 1923 to 1948, as well as in previously published etiological studies in the literature, the only constant finding has been the older age of the mothers of mongols. No evidence has been found to support the view that mongolism might be hereditary. There is no indication for eugenic precautions in the case of women who have had one mongol child, for the risk of their having another mongol child is not significantly greater than that risk for other women of the same age group. It seems clear that various exogenous maternal factors play a part in the occurrence of mongolism, primarily the more advanced age of the mothers and the depressed reproductive faculty in these women. There is room for intensive continued research on the etiology of mongolism.

Toxoplasmosis as Cause of Mongolism. H. O. Kleine. Ztschr. Geburtsh. u. Gynäk. 147:13-27 (No. 1) 1956 (In German) [Stuttgart, Germany].

Kleine demonstrates on the basis of three cases that mongolism is a special form of connatal toxoplasmosis or at least that it can be caused by toxoplasmosis, because he has observed other cases of mongolism in which the mother had a virus infection during the first three months of pregnancy or cases in which rhesus factor incompatibility played a part. He emphasizes the role of toxoplasmosis and regards it as the most frequent cause. He mentions the following factors as evidence that a toxoplasmogenic embryopathy played a part in the three cases reviewed: 1. The mothers gave strongly positive Sabin-Feldman tests and had roentgenologically demonstrable foci of cerebral calcification as well as pigmentations in the eyegrounds. 2. The infants had nystagmus, strabismus, and encephalitis, and one of the mongoloids had an auricular attachment as an accompanying malformation. The fact that "accompanying defects" are the same in toxoplasmosis and mongolism is further evidence of a causal relation between these two diseases, and such defects aid in establishing the period in intrauterine development during which toxoplasmosis produces the characteristics of mongolism. The damage to the embryo during the "organogenetic" period and the concepts of "embryopathy" versus "fetopathy" are discussed. The first three months of gestation are the period of organogenesis, and it is important that the head and brain develop ahead of the other organs. Intrauterine damage is the more severe, the earlier it develops during the period of gestation. The simultaneous appearance of apparently unconnected defects, for instance the simultaneous occurrence of feeblemindedness and syndactylism or the combination of a defect in the cardiac septum and the absence of the middle phalanx of the fifth finger in mongolism can be explained by damage to centers of organization during the early embryonal period. According to the author's theory, mongolism is an exogenic disturbance in development elicited by a diaplacental infection with toxoplasmosis of an embryo still in the phase of organogenesis, that is, during the first three months of gestation.

The fact that the origin is exogenic and not hereditary is highly important, because it makes prophylaxis possible. Expectant mothers or those likely to conceive should avoid contact with foods or articles that have been contaminated by mice or rats. They should avoid all contact with dogs, cats, rabbits, chickens, ducks, pigeons, sheep, and cows, because these animals are the chief hosts of Toxoplasma. In these animals toxoplasma usually produces intestinal ulcerations, but it may also cause bronchopneumonia and meningitis. This form of prophylaxis is the more important because the therapeutic outlook for mongolism is hopeless.

Malignant Diphtheria. M. Rizzardini and O. Undurraga. Rev. chilena pediat. 27:242-236 (June) 1956 (In Spanish) [Santiago, Chile].

Nineteen children of either sex with malignant diphtheria were observed in a pediatric hospital department for infectious diseases between the years 1946 and 1954. Most of the patients were between the ages of 6 and 12 years. They were hospitalized on the second or third day of the disease. They were acutely ill, with symptoms of acute toxemia, extensive necrotic or hemorrhagic pseudomembranes, purpura, great tumefaction of the neck, and renal and cardiovascular complications. The treatment consisted of the administration of diphtheria antitoxin, in an average total dose of 80,000 units, and of antibiotics. None of the patients survived. Autopsy was performed on 17. The diagnosis of diphtheria was confirmed. In 50% of the cases the membranes invaded the buccopharyngeal cavity, the larynx, the trachea, and, in some cases, the branches of the bronchi. The heart and kidneys were the structures most constantly damaged. Malignant diphtheria can be differentiated from the acute forms of diphtheria. The acute toxemia causes the patient to be greatly excited at certain moments and stuporous at others. The disease, which does not respond to any treatment, such as early administration of large or repeated doses of diphtheria antitoxin, alone or with antibiotics, follows a rapid course, with a mortality of 100%.

A Clinical and Biochemical Study of Galactosaemia: A Possible Explanation of the Nature of the Biochemical Lesion. G. M. Komrower, V. Schwarz, A. Holzel and L. Goldberg. Arch. Dis. Childhood 31:254-264 (Aug.) 1956 [London, England].

The authors report two new cases of galactosemia in children born in 1951 and 1953 respectively. The results of clinical and biochemical investigations and the effect of milk or galactose feeding for 8-or-10-day periods are described, with particular reference to blood glucose and galactose levels, galactose excretion, renal function, and blood and plasma phosphorus levels. Reference is made to the work carried out on certain aspects of erythrocyte metabolism in this disease. The causation of the signs and symptoms of the disease is discussed in the light of the findings reported in this communication. The hypothesis is put forward that the varied manifestations of galactosemia may be attributed to localized accumulation of galactose-1-phosphate within the tissues and that the extent to which such accumulation occurs—and consequently the resulting lesion or impairment of function—is determined by the ratio of local concentration of enzymes concerned with the early stage of galactose metabolism. More than 40 cases of galactosemia have been described in the literature. Galactose has always been implicated as the toxic agent, and the development of hepatomegaly, jaundice, cataract, mental retardation, proteinuria, and, more recently, aminoaciduria, have been attributed to the damaging effect of this sugar on each of the organs concerned.

Free Diets in the Treatment of Diabetic Children. C. C. Forsyth and W. W. Payne. Arch. Dis. Childhood 31:245-253 (Aug.) 1956 [London, England].

The clinic for diabetic children at the Hospital for Sick Children, Great Ormond Street, London, was started in 1926. Initially, strictly weighed diets were used with a carbohydrate content of up to 100 gm. daily. It soon became apparent, however, that many of the children were hungry and that they were not growing well. The food intakes were gradually increased until normal in quantity, and in 1936 free diets were tried for the first time. Concentrated carbohydrates, such as table sugar, jam, chocolate, and sweets, are restricted, but unlimited quantities of plain fare are provided. Cooperation is excellent with regard to the regularity of meals, because the importance of avoiding insulin reactions is soon appreciated, and when the diets are analyzed they are remarkably similar from day to day. Although the diet employed is not truly free, there is a real difference between such a simple diet and a strictly weighed diet.

This paper deals only with patients regularly attending the clinic and those who came for examination in response to a letter and were still on a free diet. The duration of diabetes exceeded 15 years in 41 of the 100 patients, and the others had been diabetic for between one and 15 years. Their ages ranged from 3 to 41 years, and the longest period on a free diet was 18 years. The patients were interviewed and examined, particularly for evidence of retinal degeneration and neurological, renal, or vascular disturbances. Except for short periods of loss of balance due usually to intercurrent infections, all patients remained entirely free from thirst, polyuria, or ketosis. Insulin reactions have been mild and hypoglycemic coma has been very rare. Growth has been satisfactory. The incidence and severity of retinitis increased with the duration of diabetes. A rise in the incidence of retinitis was noted only in patients failing to satisfy the standard of control for more than half of their period of diabetes. Because the over-all results of treatment have been as good as those obtained by clinics employing weighed diets and because of the psychological advantages and the better cooperation achieved, the authors believe that the use of a liberal diet will permit the best control in the greatest number of children.

Gastrointestinal Allergy to Cow's Milk in the Neonatal Period. R. B. Tudor. Journal-Lancet 76: 245-246 (Sept.) 1956 [Minneapolis].

Manifestations of gastrointestinal allergy in children are most commonly due to cow's milk. The first allergic symptoms usually occur from birth to 4 months of age. At this time, the intestine may be sensitive when the skin is not. Skin testing is usually inconclusive. The most common symptoms of gastrointestinal allergy due to cow's milk are colic, vomiting, diarrhea, nasal stuffiness, cough, wheezing, and shock. Unless the child is sensitive to the lactalbumin of cow's milk, goat's milk is not a successful substitute because the casein in cow's milk and goat's milk is identical. Soy bean milk, a weak sensitizing protein, is usually the best milk substitute. The author presents histories of seven infants with symptoms of gastrointestinal allergy due to cow's milk. Most of them improved when soy bean milk was substituted for cow's milk. One required a meat base formula, and another had no further difficulty when goat's milk was substituted for cow's milk.

Idiopathic Hypercalcaemia. W. Kidney. J. Irish M. A. 39:64-67 (Sept.) 1956 [Dublin, Ireland].

Idiopathic hypercalcemia occurs in infancy and early childhood and is associated with an increase in serum calcium and blood urea levels. The chief symptoms are inadequate food intake and vomiting, which result in failure to thrive, wasting, constipation, hypotonia, and lethargy. The child is usually small, undernourished, pale or pink, flabby, and quiet or dull. The age is usually over 4 months and under 2 years at the time of onset. The child may be mistaken for a cretin. The facial characteristics are marked epicanthic folds, overhanging upper lip, wide mouth, large lower lip, low-set ears ("elfin" look), and sometimes squint. Depositions of calcium may occur, particularly in the kidneys, giving rise to persistent infection. Idiopathic hypercalcemia must be differentiated from such conditions as pyelitis, renal rickets, pink disease, Albers-Schönberg disease (osteopetrosis), renal acidosis, and Fanconi's nondiabetic glycosuria.

The author describes observations on 13 children with idiopathic hypercalcemia. Children with the mild form may recover in a few months or years, but in those with the severe form physical and mental retardation, stunting, and deposition of calcium in the lungs, muscles, and kidneys may finally lead to death. There is no specific treatment, but elimination of vitamin D may be tried, because the child may have received excessive doses or may be hypersensitive to normal doses. Reduction of calcium intake by the elimination of cow's milk, which contains four times as much calcium as does human milk, may be desirable. Cortisone or one of its modifications usually produces great improvement, but it is too early to decide whether it will prevent the mental retardation so often found in the chronic form of idiopathic hypercalcemia.

UROLOGY

The Resemblance of Hypertrophy of the Prostate to Congenital Polycystic Disease: Reconstruction of Cystic Lesions of Hypertrophied Prostate in Three Cases. R. F. Norris, V. E. Martens and R. W. O'Gara. J. Urol. 76:276-286 (Sept.) 1956 [Baltimore].

The similarity of the lesions of hypertrophy of the prostate and of polycystic disease of the newborn is described, and the lesions in the prostate are illustrated by means of reconstructions from serial sections in three patients. The first prostate was selected for study because it was considered typical of a man in early middle age. The areas of glandular enlargement were localized and not extensive. In the serial sections studied, none of the enlarged glands were seen to be isolated as cysts. The second prostate was selected because it showed a preponderance of glandular hyperplasia and the third because of a preponderance of fibromuscular hyperplasia. Neither gland was unduly enlarged. Greatly hypertrophied prostates were not chosen for study because it was feared that the first changes in structure might be obscured in advanced stages of the disease. As regards polycystic disease of the newborn, evidence has previously been presented by the senior author (R. F. Norris) and his collaborators to show that the embryologic development and differentiation of polycystic organs progresses while the cystic lesions are being formed. As a consequence of the epithelial cystic proliferation, the ducts or epithelial tubules eventually are pinched off as isolated segments or as dilated cysts. This sequence of changes resembles the phenomenon of normal resorption of the provisional organ, the mesonephros. In the latter instance, segmentation of tubules and isolation of glomeruli as cysts normally precede the resorption of these elements as the mesonephros degenerates. Since the first generations of tubules in the metanephros are also thought to be normally provisional, the authors suggest that segmentation and cystic dilatation of the tubules in polycystic disease of the kidney and of other organs represent an extension of this normal process of resorption to a pathological degree. The epithelial lesions of the hypertrophied prostate characterized by cystic dilatation of ducts and acini and by the isolation of blindly-ending cystic complexes resemble the lesions of congenital polycystic disease.

The objection may be raised that polycystic disease of the newborn differs from hypertrophy of the prostate in the short time required for its development. This difference may be more apparent than real if the rapidity of all embryologic development is taken into consideration. So far as the authors know, neither polycystic disease nor hypertrophy of the prostate has been reproduced experimentally in animals. The cause of each disease, therefore, is obscure. Whether there are etiological factors in common is still unknown, but in the case of hypertrophy of the prostate, the belief persists that imbalance of endocrine secretions is the cause of the disease. Endocrine disturbances during pregnancy, however, have not been extensively investigated as a cause of polycystic disease. The conclusion seems warranted that the similarity of the lesions of hypertrophy of the prostate to those of congenital polycystic disease is important not only because lesions of embryologic development can be mimicked in the organs of adults, but also because the two diseases may have etiological factors in common.

Congenital Renal Aplasia with Calcified Cystic Degeneration: Report of Two Cases and Review of the Literature. B. S. Abeshouse. J. Internat. Coll. Surgeons 26:283-296 (Sept.) 1956 [Chicago].

The author has collected 16 cases of extensive calcification of cysts in congenitally aplastic kidneys. He describes two additional cases of this unilateral condition in a 40-year-old woman and a 78-year-old man. Analysis of the literature on congenital renal aplasia with and without cystic degeneration and of the observations made in the two patients with congenital aplastic kidneys containing calcified cysts warrants the following conclusions: 1. There is a definite need for an exact definition of the three important congenital anomalies of renal structure, i. e., agenesis, hypoplasia, and aplasia, to enable the urologist and pathologist to diagnose and classify the cases properly. 2. The distinguishing clinical and pathological features of renal agenesis, hypoplasia, and aplasia permit an accurate differential diagnosis, which may be made with the aid of cystoscopic studies, excretion tests with indigo carmine and phenolsulphonphthalein, and roentgenographic studies, particularly excretory urography and retrograde pyelography.

Renal aplasia is characterized by a total lack of definite renal anatomic form and physiological function in infants and children. In adolescents and adults the aplastic kidney may exhibit marked cystic degeneration, apparently the result of arrested development in the metanephric stage. In one patient total excision of the retroperitoneal mass was carried out. Microscopic sections through the cyst wall showed groups of vestigial tubular structures lined in part by pseudostratified tall cuboidal epithelium. There were also scattered small cysts. The cysts were encased in a dense collagenous fibrous tissue. There were foci of calcium deposition as well as of osseous tissue formation. Renal aplasia associated with cystic degeneration has also been described as multicystic or congenital cystic hypoplasia and not infrequently confused with unilateral polycystic kidney and multiple serous cysts of the kidney. The pathogenic and pathological aspects of calcification, ossification, and cartilage in the walls of the cystic type of aplastic kidney are discussed.

Local Hydrocortisone for Hunner's Ulcer of the Bladder. J. H. Johnston. Brit. M. J. 2:698-699 (Sept. 22) 1956 [London, England].

The patients treated were women aged 63, 68, and 73 years in whom interstitial cystitis with ulceration (Hunner's ulcer) had existed for from two to six years. Treatment by bladder distension with the patient under anesthesia, zinc ionization, and vesical irrigation had formerly been carried out on many occasions. In January, 1956, each was treated by cystoscopic injection of hydrocortisone into the bladder. All have shown marked symptomatic improvement beginning a few days after the injection. The total duration of the remission produced by this therapy is not known, but it is to be expected that, when symptoms recur, further infiltration of the bladder musculature will again be effective. The author learned that Schulte and Reynolds obtained satisfactory results with a similar technique using hydrocortisone and hyaluronidase.

OPHTHALMOLOGY

Report on 104 Cases of Glaucoma Operated upon by Galvano-Cautery Puncture. R. Colley. Brit. J. Ophthal. 40:436-438 (July) 1956 [London, England].

Colley performed the first galvanocautery puncture on July 27, 1950, and since that date all patients with glaucoma of whatever type admitted to his care at the Bath Eye Infirmary for operation have been treated by this procedure. In all, 121 galvanocautery punctures were performed on 104 eyes—100 by the author himself and 21 by an assistant. Fifty-four of the operations were performed in chronic simple glaucoma, 34 in acute or subacute glaucoma, and 33 in secondary glaucoma. Local anesthesia was used in 72 and general anesthesia in 49 operations. The operative technique used was a slight modification of the galvanocautery puncture described by Preziozi in 1924 and in 1950. The results in chronic, simple, acute, and subacute glaucoma appeared to be as successful as those obtained with most other operations. In cases of secondary glaucoma—apart from those due to uveitis—the results were very poor.

Although the number of patients operated upon is insufficient for final conclusions, Colley feels that Preziozi's galvanocautery puncture is worth a more extensive trial. It is very similar to Elliott's trephine operation, but is even easier to perform and takes a shorter time. Other advantages of the galvanocautery puncture are that it can be performed under local anesthesia, especially in old or ill patients, and that the slow escape of the aqueous when the limbus is pierced makes an intraocular hemorrhage very unlikely.

Water-Drinking and Tonography in the Diagnosis of Glaucoma. B. Becker and R. E. Christensen. A. M. A. Arch. Ophth. 56: 321-326 (Sept.) 1956 [Chicago].

Although characteristic field loss and cupping of the optic nerve head establish the diagnosis of glaucoma, therapeutic efforts in the chronic simple variety of this disease depend upon early detection. Methods available for its diagnosis include tonometry, provocative tests, and tonography. The fact that glaucomatous eyes can demonstrate decreased facility of outflow in the absence of elevated intraocular pressure accounts for their earlier recognition by tonography than by tonometry. When tonography was combined with provocative tests, it was noted that some glaucomatous eyes responded with induced impairment of outflow facility in spite of a failure of this procedure to provoke a rise in intraocular pressure. Thus, tonography before and after water-drinking provided a more sensitive method for the detection of glaucoma than did either alone. A comparison is presented of tonometry, water-drinking, and tonography on 175 normal eyes and 188 eyes with chronic simple (open-angle) glaucoma and loss of visual field. The two groups of eyes could best be separated on the basis of data obtained from tonographic tracings one hour after drinking 1 liter of water.

INDUSTRIAL MEDICINE

An Occupational Agent (N-Butyraldoxime) Causing Reaction to Alcohol. W. Lewis and L. Schwartz. M. Ann. District of Columbia. 25:485-490 (Sept.) 1956 [Washington].

An unpleasant reaction after the ingestion of small amounts of alcohol was noted recently in a large printing company. The agent that is absorbed into the body and "sensitizes" the printers is known as the antioxidant N-butyraldoxime. After such "sensitization" the response to alcohol consisted of a reddish, violescent, nonitching, coalescing, macular rash of the face, neck, and upper trunk; congestion of the conjunctiva and nares; congestion of the mucous membranes of the throat, which caused dyspnea without wheezing, and palpitation. The "reaction" to alcohol caused by N-butyraldoxime is similar to but milder than the Antabuse-alcohol reaction. The blood acetaldehyde level, which is elevated by the absorption of N-butyraldoxime, is further markedly elevated shortly after the ingestion of alcohol, and this causes the unusual "reaction." The effects of exposure to N-butyraldoxime largely disappear in 24 hours. Apparently no permanent damage is done to the body by the new agent. A new "cure for alcoholism" may have been found.

THERAPEUTICS

A Class Experiment on Ganglion Block in Human Subjects. W. D. M. Paton and H. Steinberg. Brit. M. J. 2:622-627 (Sept. 15) 1956 [London, England].

The pharmacology class at University College Hospital in London provided an opportunity whereby some knowledge about the action of ganglion-blocking agents could be obtained in a population of healthy young adults, at the same time receiving training in making clinical observations and in rendering these observations quantitative. The students worked in groups of four, with one student as subject and the remaining three as observers dividing the various duties among themselves. A set of observations was made every 20 minutes, *timed* with a stop-clock, in the following order: supine blood pressure and pulse rate; standing blood pressure and pulse rate; skin temperature, body temperature, and room temperature; salivary secretion and sweating rate; ocular accommodation and reaction to light. This sequence was strictly followed, so that the interval between successive particular types of observation was kept constant. Two sets of control observations were made before injection of the drug, the subject having been instructed to take a light lunch, not to drink too much, and to empty his bladder. Immediately after the second set of control observations, 25 mg. of hexamethonium bromide was injected subcutaneously into the deltoid area.

The most common effect was a fall in body temperature (90% incidence) and rise in skin temperature (76%); and then (in descending order of frequency), fall in supine and standing systolic blood pressure, rise in supine and standing pulse rate and reduction in salivary secretion, and reduction in the reaction of the pupil to light and to accommodation (30-40% incidence). Sweating was also reduced. The incidence of ganglionic block over the various autonomic functions tested was different in every one of the 41 subjects for whom complete records were obtained. Variability in the response to a ganglion-blocking agent is as great in normal subjects as in patients. It may be regarded as a result of the varying autonomic constitution of different individuals.

Acute Renal Failure During Pentolinium Therapy. A. B. Carter and R. W. Payne. Lancet 2:537-539 (Sept. 15) 1956 [London, England].

Carter and Payne report the histories of two men, aged 69 and 46, respectively, in whom acute renal failure developed while they were being treated for hypertension with pentolinium tartrate (Ansolysen). The type of renal failure suggested an initial lowered filtration rate associated with prolonged hypotension followed by failure of tubular function. These two cases suggest that the continued use of pentolinium tartrate may be dangerous to elderly patients, although the usual side-effects of postural vertigo, constipation, and dryness of mouth may be absent. The use of pentolinium in the elderly can be justified only as a life-saving measure in cases of left ventricular failure, progressive gross retinal changes, or continuing hypertensive encephalopathy. The patient should be instructed to watch for listlessness, drowsiness, or any diminution in volume of urine and thereupon to stop taking the tablets. Once renal failure is suspected in a patient receiving pentolinium tartrate and the drug has been withdrawn, it is important to restore circulation as quickly as possible by raising the blood pressure. An intramuscular injection of 10 mg. of methedrine sulphate was effective in each case. Care should be used in prescribing larger doses because hypertensive patients remain very susceptible to methedrine even when they are in hypotension. Once the blood pressure has become reasonable, the treatment should be as for anuria from other causes.

Breast Cancer and Heptaldehyde (Preliminary Report). R. N. Lawson, A. L. Saunders and R. D. Cowen. Canad. M. A. J. 75: 486-488 (Sept. 15) 1956 [Toronto, Canada].

The rarity of cancer of the breast in Eskimo women in Canada has led to an investigation of their mode of life. The most striking aspect of their diet is the high proportion of fat, much of which is consumed in a frankly rancid state. Heptaldehyde is one of the chemical factors found in rancid fat. Earlier investigators had observed that when this substance is added to the diet of mice harboring spontaneous carcinomas of the mammary gland, liquefaction and regressive changes of the tumors resulted without apparent injury to the animals. The authors studied the toxicity of heptaldehyde in rats, demonstrating the fact that the lethal dose in 200-gm. rats was between 4 and 5 cc. They have given over 300 doses of 1 cc. each to human patients without any apparent ill-effects. They have used as much as 3 cc. but have confined the maximum quantity to 1 cc. in any single injection site.

Two patients with inoperable metastatic breast cancer were given intragluteal injections of heptaldehyde at intervals of one week. Both patients experienced a painful response in the site of the malignant tumor within five minutes of the intragluteal injection. The areas of the breast surrounding the tumor did not become tender. Tumor growth appeared to be immediately arrested. After eight weeks, treatment was discontinued, as the pain phenomenon in the tumors was cumulative. Tenderness and pain in the tumor nodules increased with repeated doses and persisted for longer periods. Three weeks after cessation of treatment, one patient was given 300 mg. of testosterone. Within 24 hours all the tumor areas visibly increased in size, and she died five days later. The other patient underwent simple mastectomy, and she is now alive and free of gross disease 10 months after treatment. Extending the studies to other patients with breast cancer, the authors found that four-fifths experienced a pain reaction within the tumor within from four to eight minutes after the injection. On several occasions when the drug inadvertently entered the blood stream, as evidenced by a rancid taste in the mouth and pain in the breast tumor, there was a distinct drop in skin temperature over the cancer within 10 minutes of the injection. Since no demonstrable thermal changes were noted after administering heptaldehyde in any case of benign or inflammatory breast disease, it would appear that this phenomenon could be a useful clinical test for breast cancer.

Symptomatology and Pathogenesis of Intoxication with Penicillin Ester. G. Wichmann, E. Koch and F. Heiss. Ztschr. klin. Med. 154:111-125 (No. 2) 1956 (In German) [Berlin, Germany].

Experiments were carried out on guinea pigs and rats given injections of the hydriodide of the diethylaminoethyl ester of penicillin by the intramuscular, intracardiac, and intracerebral routes and into the carotid arteries. Similar experiments had previously been made with sodium penicillin G. Three standard syndromes of intoxication were observed in both guinea pigs and rats after the administration of the penicillin ester: acute generalized tonic-clonic spasms, acute diffuse pulmonary edema with pulmonary hemorrhages, and enterocolitis with a protracted course and terminal collapse. Acute generalized spasms and acute pulmonary edema were produced in the animals by the intramuscular administration of the penicillin ester, but these acute syndromes were not produced when sodium penicillin G was given by this route; they were, however, produced by both penicillin ester and sodium penicillin G when given by the intracerebral route or into the carotid arteries. The severity of the intoxication syndrome that occurred in the animals after the administration of the penicillin ester always depended on the degree of concentration of the penicillin ester in the cerebral tissue. It appears that the penicillin ester passes the blood-brain barrier in the animals and that the penicillinase activity in the cerebral tissue is temporarily inhibited. The results are a breaking-down of ganglion cells, acute spasm syndromes, and pulmonary edema. A review of the literature showed that after the administration of penicillin ester preparations to human beings the incidence of symptoms of intoxication was 130 times higher than after the administration of procaine penicillin preparations.

Jensen and Hallas-Moller and his Danish co-workers reported that the concentration of the penicillin ester in the pulmonary tissue of guinea pigs was three times higher than that in the blood, while the pulmonary tissue concentration of the penicillin G alone, which has an antibiotic effect apart from the ester compound, was not higher than its concentration in the blood. The authors' observations in the course of their experiments in animals and reports in the literature of observations in man establish the fact that the pulmonary affinity for the penicillin ester in animals and in man applies only to the ester itself, while the concentration of the penicillin freed from the ester compound is about the same in the pulmonary tissue and in the blood.

Penicillin ester preparations have been recommended for the treatment of patients with inflammatory cerebral disturbances, pneumococcic and meningococcic meningitis, and inflammatory diseases of the lungs. From the viewpoint of the greatest usefulness and the least damage, penicillin ester preparations are definitely inferior to sodium penicillin G in the treatment of all of these diseases.

ANESTHESIA

Roentgen Therapy and Cyclopropane Sensitivity. P. A. Foster. Anesthesiology 17:735-738 (Sept.-Oct.) 1956 [Philadelphia].

A 39-year-old man received a course of deep roentgen therapy for carcinoma of the floor of the mouth. The irradiation was completed five weeks before an operation was scheduled. There had been no radiation sickness, and the patient had been able to eat, had not lost much weight, and was in good general condition. A two-stage operation was planned in which suitable skin pedicle grafts would first be fashioned for use at the second stage when reconstruction of the lower jaw was to be carried out after resection of part of the mandible. It proved impossible to maintain this patient on cyclopropane because of extreme sensitivity. After a flow of this gas of 200 ml. per minute had been allowed to enter the closed circuit for two or three minutes, respiratory arrest followed that lasted for approximately half an hour. Pulse and blood pressure, however, were relatively unaffected. Eventually, the use of cyclopropane was discontinued, and nitrous oxide with minimal ether, and Demerol intravenously, was substituted. He did not prove unduly sensitive to this combination, tolerating amounts that experience suggested was normal for a person of his age and sex. Recovery was uneventful after the surgery, which took five and one-half hours.

An extreme sensitivity to cyclopropane may be shown by elderly people, especially if their premedication has included a respiratory depressant, but it is not usually seen in younger adults. The selective depression of respiration with poor analgesia in this 39-year-old man is regarded as significant because it has been observed that animals exposed to roentgenization of the whole body show an especially poor tolerance for cyclopropane but not for ether, ethylene, nitrous oxide, or thiopental sodium. Radiation therapy would probably not have such an effect on human beings unless the cerebrospinal axis is in the path of the beam. It is suggested that irradiation around the head may increase the permeability of intracranial vessels, thereby allowing entry to certain drugs (for example, relaxants) that are normally excluded by the blood-brain barrier. Drugs that normally penetrate may do so in greater degree. The peculiar pattern of neuronal radiation damage seen suggests that an excessive vagal tone may increase the hazards of intubation with cyclopropane, that consciousness may be more easily depressed, and that disturbances of temperature regulation may be encountered. Unusual responses to anesthesia following radiation therapy have received little attention in the literature. They may prove important during the treatment of casualties following an atomic explosion.

Control of Postoperative Vomiting with Marezine: A Double Blind Study. D. C. Moore, L. D. Bridenbaugh, V. F. Piccioni and others. Anesthesiology 17:690-695 (Sept.-Oct. 1956 [Philadelphia].

The effectiveness of parenteral injections of Marezine (cyclizine lactate) to control postoperative vomiting was investigated with a method that has been developed as a standard for antiemetic drugs. The cyclizine is injected intramuscularly when the patient is taken to the operating room, again intramuscularly on return from the operating room, and then intramuscularly every four hours for four doses. In this experiment, 1 cc. of solution was injected each time. The cyclizine solution contained 50 mg. of the drug per cubic centimeter. During a double-blind study on 276 patients, who were operated on under various types of anesthesia, it became evident that cyclizine lactate significantly reduced the incidence of postoperative vomiting. This would seem to substantiate previous reports, which had asserted the effectiveness of cyclizine but had not employed the double-blind technique in evaluating the drug.

BOOK REVIEWS

Medical Effects of the Atomic Bomb in Japan. Edited by Ashley W. Oughterson, Clinical Professor of Surgery, Yale University School of Medicine, New Haven, and Shields Warren, Pathologist, New England Deaconess Hospital, Boston. National Nuclear Energy Series. Manhattan Project Technical Section, Division VIII—Volume 8. Cloth. $8. Pp. 477, with illustrations. McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 36; 95 Farringdon St., London, E.C.4, England, 1956.

This well-illustrated and well-documented book concerning the medical effects of weapons that have altered history and our way of life should be of great interest to physicians throughout the world. The first chapter contains an excellent summary of findings, which are afterward documented in detail in appropriate chapters. The book is fairly comprehensive in that it describes the prelude to the work and the scope of damage and effects on medical care and facilities, presents statistical data on population and casualties, and discusses medical aspects from the viewpoint of the clinical observer, the hematologist, and the pathologist. Six appendixes, dealing with subjects such as organization and personnel, materials and methods, population, and statistical data, afford more specific information concerning the studies reported in the text. The index is weak. The book is literally crowded with facts and material that one may study for hours. Perusal of the summary chapter and selected reading of other portions will rapidly acquaint the medical reader with the general and specific medical problems of nuclear warfare. The colored plates vividly depict the injuries. Some of the photographs are reproduced from early Japanese military reports which illustrate early findings that United States survey personnel did not observe because of their arrival in the areas weeks after the bombings. This is a valuable book for background and reference for physicians concerned with the medical aspects of nuclear warfare and, in addition, for persons engaged in military medicine, which includes those who are concerned or who should be concerned with the medical aspects of civil defense—namely, all physicians.

The Administration of Health Insurance in Canada. By Malcolm G. Taylor. Cloth. $5.65. Pp. 270, with 5 illustrations. Oxford University Press, 114 Fifth Ave., New York 11; Amen House, Toronto, Canada, Amen House, Warwick Sq., London, E.C.4, England, 1956.

Today about 50% of Canada's population is enrolled in some type of health insurance plan. With attention concentrated primarily on the Blue Cross hospital care plans, the medical care plans sponsored by the provincial medical associations, and the hospital and social assistance medical care programs operated by the government, this study encompasses a total of 24 specific insurance plans. An evaluation of the various plans is based on detailed examination and description of the differing objectives, achievements, and problems of each type of plan. In developing his central theme of the task of administering health insurance, the author discusses extensively such matters as the determination of benefits and premiums and the effects of the individual plans on the physicians, hospitals, and patients involved. The author's personal observation provides the principal basis for a substantial part of the text. The 38 tables and figures that appear in the book and the numerous text tables serve as helpful supplements to the written text. Much of the tabulated material, however, is not fully documented with specific references to exact sources and/or to the author's method in arriving at statistics.

The Canadian Blue Cross plans, modeled after those developed in the United States, operate on the service benefit principle whereby a maximum number of days of hospital care per year plus necessary extras (operating room, drugs, and dressings) are provided. The five Blue Cross plans operative in Canada are coordinated by the Canadian Council of Blue Cross Plans. In addition to their hospital care benefits, three of the plans offer a limited medical and surgical benefits contract of the indemnity type. In 1954 about 3,255,000 people were enrolled in Blue Cross plans for hospital benefits, and 1,027,000 for medical and surgical indemnity benefits. The profession-sponsored medical care plans also provide benefits on a service basis. In contrast to most of the profession-sponsored plans in the United States, many of the Canadian plans offer home and office calls by physicians as benefits. The physicians accept a 10% reduction in fees to cover administrative costs. These plans cover 1,353,000 persons. Government-sponsored hospital care plans have been established in four Canadian provinces in which total enrollment in 1954 was 2,696,000 persons. The Swift Current Medical Care Plan is the only example of a government-sponsored program covering all the residents of a large area (about 50,000 people in southeastern Saskatchewan reside in the region served by the Swift plan). This comprehensive medical care program is supported by taxes levied on all residents and provides payment to physicians on a fee-for-service, contract-schedule basis. Public medical care plans apply only to those groups in the population receiving social assistance of some sort. The number of such beneficiaries in 1953-1954 was 293,792.

One of the most serious problems facing government-sponsored plans concerns enrollment, which must necessarily encompass the entire population. The absence of the promotional function does not counteract the obstacles that obligatory comprehensive and simultaneous registration and tax payment present. In Canada today, all of the 10 provinces exercise some degree of supervision over all of the hospital and medical care programs. While the amount and type of supervision varies from province to province, in the author's opinion, successful administration will soon necessitate a degree of uniformity. Taylor describes the position of the physician in private practice as "anomalous"—on the one hand, he is a confidant and an alleviator of pain, on the other hand, he "is a prime example of the small businessman with fixed and variable costs in operating his practice whose income is the difference between his revenue and expenditures." In the author's thinking, these two functions tend to conflict. He believes that the physician, in asking remuneration for his services, counteracts his beneficial work by inciting worry, fear, and "continuance of the state of ill-health." In respect to this, Taylor quotes Stern who says, "the attitude of the lay public is that the physician is the beneficiary of another's misery." It is on the basis of this premise that the main criticism of the book can be promulgated. While the physician feels entitled to just remuneration, his primary role is that of a professional servant and not that of a tradesman or businessman. To equate the two roles is to misinterpret the function of the private physician, as well as to miscalculate his own conception of his role in society. Although an economic factor does exist in the doctor-patient relationship, it can be contended that this element is subordinate to the quality of care that the physician strives to provide.

Taylor points out that administrative regulations are time-consuming and irritating to the physician, but he also implies that such disadvantages are offset by the advantages of being able to offer whatever treatment the physician believes necessary without concern over the patients' ability to pay. It should be remembered that this advantage is greatly limited by the extent of the patients' insurance coverage. In conclusion, the author points out that governmental controls are the lesser of two evils, the greater being unpredictable and frequently unmanageable medical bills. This view would appear to be an oversimplification of the problem. Aside from the inevitability of the economic factor in medical care (which is an essential factor regardless of whether health insurance is available), the principal problem to be resolved in regard to health insurance would seemingly involve an evaluation of the effect of controls on the quality of medical care. Physicians believe that further controls would be detrimental, indicating that Taylor's "two evils" have been ill-defined. The medical profession believes that any form of contractual practice is unethical to the extent that it results in a deterioration of the quality of the medical services rendered; thus, the effects of increased nonmedical control on the quality of medical care seem to the physician an unreasonably high price to pay for the opportunity to "budget medical care expenditures."

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

Techniques and Procedures of Anesthesia. By John Adriani, M.D., Director, Department of Anesthesiology, Charity Hospital, New Orleans. Second edition. Cloth. $8.75. Pp. 568, with 192 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto, 2B, Canada, 1956.

This second revised edition of a popular textbook follows the purpose of the first edition, namely, to provide an outline for students of anesthesiology. The important points are presented in a concise but comprehensive manner. The text is divided into 10 parts. The first consists, after a few definitions, of tables giving the general properties of anesthetic drugs, and suggestions for selecting procedures of giving anesthetics for operations on the different regions of the body and drugs to be used when the most commonly encountered clinical conditions are met. Much of this material is from the author's book, "Selection of Anesthesia." The recommendations made are presented in outline form, and the justification for them is supported not by discussion but simply with a brief remark. This part also includes discussion of preanesthetic medication, a subject presently undergoing radical changes with the introduction of new drugs and new concepts. The recommendations given here reflect the recent teaching on this subject but not necessarily the latest methods. There is also a discussion of records of anesthesia and their preparation.

The second part is devoted to inhalation anesthesia. It briefly describes the drugs used and particularly the appliances. The use of the latter is covered in some detail with many photographic illustrations. This section covers the use of endotracheal equipment also. The classic signs of anesthesia of Guedel are given, although in present practices they alone are not sufficient to guide the clinician in determining the depth of anesthesia. The third part covers the complications of anesthesia and gives sound recommendations for avoiding and managing them. Basal narcosis with intravenous injections and rectal anesthesia are the subjects of the next two parts, followed by a section on regional anesthesia. Although this section covers one-fifth of the book and is fairly well illustrated, it provides the student with too little information to be of much value. Many of the most recent practices have not been included and some of the recommendations are debatable. For example, the author implies that blocks, excepting skin wheals, are best done with 22-gauge or larger size needles.

Specialized procedures occupy the next part, including pediatric, geriatric, thoracic, and obstetric methods. Little can be done with any of these subjects within the limited space allotted, therefore the text attempts little more than an outline of suggested procedures that are essentially the same as those already described. Recovery rooms are given some space in the final pages of this section. In the last two parts, resuscitation and inhalation therapy are considered. There is an appendix with clinical laboratory values and a good index. A brief bibliography is found at the end of each discussion. The illustrations show various types of equipment and their use. The book is an example of excellent design and printing. The author is to be congratulated on packing into so few pages the vast number of subjects included. Although the outline form will appeal to many, the book will probably be most useful to those beginning the study of this subject and possibly to those anticipating examinations by qualifying boards.

Epilepsy and the Law: A Proposal for Legal Reform in the Light of Medical Progress. By Roscoe L. Barrow, Dean, University of Cincinnati College of Law, Cincinnati, and Howard D. Fabing, M.D., Chairman, Legislation Committee, American League against Epilepsy. Cloth. $5.50. Pp. 177. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1956.

This book is described on the title page as being "a proposal for legal reform in the light of medical progress," but Dr. Pearce Bailey, in his foreword, recognizes that, for all its scholarship, this book is part of the literature of indignation. If all who read the book are as aware as was Dr. Bailey of the easily discernible use of half-truths and innuendo in seeking to appeal to the reader's emotions, then more good than harm should come from a widespread reading of it. The authors sincerely contend that medical progress in the control of epileptic seizures has outmoded our epilepsy laws. Four principal areas of complaint are covered: marriage license laws, sterilization laws, driver's license laws, and workmen's compensation laws. The best case is made for the first two. From the material presented, there seems to be little doubt that epilepsy is not the same as idiocy and insanity and that there is no eugenic reason for treating them in the same manner. It also appears that epilepsy is not an inherited disease. Society, therefore, will not suffer by permitting epileptics to marry and by eliminating epileptics from the purview of the eugenic sterilization laws. Granting the foregoing and granting that down through the years an unfortunate social stigma has attached to epilepsy, the authors are not able to present quite as good a case for amending the driver's license or workman's compensation laws. A driver who has an epileptic attack while driving 60 mph on a busy highway and an epileptic who drops one end of a heavy box that he is lifting with a fellow employee can cause serious injury to those other than himself. More than mere social stigma is involved. The authors do, however, insist that the privileges that they seek for the epileptic must be limited to the epileptic who is free from seizures and under a physician's care. Like most "literature of indignation," this book will find violent supporters and violent opponents. On the whole, however, it furnishes a valuable addition to the literature on the subject and may help to elevate the status of the epileptic in some degree. The appendix contains examples of the type of laws the authors believe should be enacted, and there is a commendably complete index, bibliography, and citation of legal references.

Management of Emotional Problems in Medical Practice. Edited by Samuel Liebman, M.D., Medical Director, North Shore Health Resort, Winnetka, Ill. Cloth. $5. Pp. 152. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; 2083 Guy St., Montreal, Canada; [British agent—Pitman Medical Publishing Co., Ltd., 39 Parker St., Kingsway, London, W.C.2, England], 1956.

This volume is the second in a series based on lectures given at the North Shore Health Resort, Winnetka, Ill., by nine distinguished physicians. Each lecture presents practical approaches to the management of the emotional problems treated daily by the medical practitioner. Dr. Karl M. Bowman's paper on psychiatric emergencies or what to do before the psychiatrist comes is full of good practical sense and gives special consideration to the violent patient and the suicidal patient, and how to manage problems of drug intoxication, refusal to eat, panic states, and hysterical states. Dr. Francis J. Gerty gives excellent advice on the use and abuse of sedatives and stimulants. Dr. Lewis Robbins considers the management of the anxious patient and takes up the symptoms, psychodynamics, and management of anxiety. The depressed patient, his understanding and management, is extremely well presented by Dr. Franklin G. Ebaugh. The management of emotional reactions in the male involutional period is covered by Dr. Otto Billig. The management of the multiple complainer by George C. Ham is an example of excellently applied practical psychiatry. Dr. Leo H. Bartemeier's paper on the management of overeating, overdrinking, and oversmoking considers overindulgence as a symptom of emotional disturbance. Dr. Walter C. Alvarez tells how to avoid the production of iatrogenic disease. He believes that anxiety neuroses are sometimes produced inadvertently by physicians and urges the physician to be optimistic, constantly to guard his tongue, especially in the presence of a hypochondriacal patient, and to avoid thinking out loud in alarming diagnostic medical terms. A concluding paper by Dr. Marc H. Hollender emphasizes the utilization of community resources in medical practice. This book is lucid, compact, practical, and clearly written. It is highly recommended.

Surgery of the Hand. By Sterling Bunnell, M.D., Consultant to Surgeon General of U. S. Army, to U. S. Navy, and to Alaska Department of Health. Third edition. Cloth. $22.50. Pp. 1079, with 1056 illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; 2083 Guy St., Montreal, Canada; Pitman Medical Publishing Co., Ltd., Pitman House, 39-41 Parker St., Kingsway, London, W.C.2, England, 1956.

The third edition of this excellent book has been greatly enlarged to include many recent advances in hand surgery. In the past, it has been through this book, as well as through the author's personal stimulus, that hand surgery has reached its present high plane. The parts dealing with the use of antibiotics for infections of the hand has been greatly expanded. Other new or improved chapters include those on postoperative treatment for the repair of tendons and on burns. The format of the book is similar to that of previous editions, but its increased size makes it a bit heavy to hold while reading. If future editions entail further expansion, the author should consider publishing it in two volumes. This book is highly recommended for all those doing hand surgery and should be in the libraries of all hospitals and medical schools. It is an excellent reference book for all levels of teaching, including the postgraduate level.

Ciba Foundation Colloquia on Ageing. Volume 2: Ageing in Transient Tissues. Editors for Ciba Foundation: G. E. W. Wolstenholme, O.B.E., M.A., M.B., and Elaine C. P. Millar, A.H.W.C., A.R.I.C. Cloth. $6.75. Pp. 263, with 96 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; J. & A. Churchill, Ltd., 104 Gloucester Pl., Portman Sq., London, W.1, England, 1956.

This small volume is the second of a series to be published annually under the auspices of the Ciba Foundation of London dealing with basic research relevant to the problems of aging. The first volume was a colloquium on general aspects of aging. The present one is devoted to the aging of transient tissues, the normal life of which is shorter than that of the organism as a whole. The program is truly international in character. The 27 participants from both the United States and abroad are eminent authorities in their respective fields of anatomy, embryology, physiology, biochemistry, biology, zoology, and botany. Those interested in aging should find delight in the comprehensive conversational manner in which the subject is covered in this symposium. It is difficult to select any one part that is more interesting than another. Perhaps those who do not feel entirely at home with the highly scientific and technical approach to the subjects presented would be engrossed especially by those parts dealing with the regenerative capacity of ovarian tissues, mitochondrial changes in different physiological states, morphological aspects of aging in the placenta, chronological changes in placental function, biochemical evidence of aging in the placenta, aging of the axillary apocrine sweat glands in women, and aging in human red blood cells. One would not do justice to this volume if particular attention were not called to the exceptional artistic merit of the illustrations accompanying the articles. The discussions of the presentations in these colloquiums lend extraordinary value and interest to the program. The informal participation by the audience and the effective but not rigid control of the symposium by the chairman might serve as a pattern for other groups, the meetings of which are so often unenlightening because of their stereotyped panel or conventional order.

Clinical Urology. Volumes I and II. By Oswald Swinney Lowsley, A.B., M.D., F.A.C.S., President and Director, Oswald Swinney Lowsley Foundation, Inc., St. Clare's Hospital, New York, and Thomas Joseph Kirwin, M.A., M.S., M.D., Professor of Urology, New York Medical College, New York City. Third edition. Cloth. $32.50. Pp. 464; 465-985, with 599 illustrations by William P. Didusch. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1956.

In this edition, chapters 1 to 5 deal with the usual, well-accepted diagnostic procedures in urology. This is followed by a good, informative chapter on anesthesiology. In chapters 7 through 34, all the various diseases of each organ of the urogenital system are discussed in a well-organized and well-documented manner. The pattern followed in the discussion of these diseases is comprehensive and to the point. Detail does not succumb to verbosity. In chapter 35 the recent advances made in the field of antibiotic therapy are discussed. Here the reader will find treated the indications, contraindications, and efficacy of the various antibiotics in the treatment of infections of the genitourinary system. Each volume contains an index to the text and illustrations. The publishers have done their part very well. The quality of the paper and the arrangement of the pages into three columns facilitates reading. Since the publication of the second edition, many advances have occurred in urology which are all well documented in this edition. These two volumes are a combination textbook, encyclopedia, and atlas of urologic pathology and surgical techniques, profusely illustrated. The present edition assures for the volumes a continuingly prominent place in urologic literature. They can be unhesitatingly recommended not only as a textbook for students, interns, and residents but also as a reference book for the practitioner, surgeon, and urologist. It is unfortunate that the death of the senior author of this edition came before he had an opportunity to see the finished product.

Electrocardiographic Test Book. Volumes I and II. Paper, loose-leaf. $5 per set. Pp. 167; 132, with illustrations. American Heart Association, Inc., 44 E. 23rd St., New York 10, 1956.

The purpose of this book is to assist students in the study of electrocardiography. The presentation in volume I consists of 110 selected electrocardiograms reproduced as examples of normal and abnormal varieties, together with questions. The answers, documented and discussed on the basis of clinical and roentgenologic data, are assembled on the corresponding pages in volume II. In addition, the two volumes contain general questions and answers pertaining to electrocardiographic differential diagnosis; tables of normal measurements, mostly compiled from the literature and some thus far unpublished; and a comprehensive index. This original approach to teaching clinical electrocardiography should serve the limited aims of the authors, although objections can be raised concerning the examples selected, the interpretation of some of the records, and the illogical questions posed in conjunction with some of the records. There are some inconsistencies in dealing with the difficult problem of differentiation of ischemic alterations from those caused by heart strain and hypertrophy (figures 3 and 24). One also wonders whether statements like the one on page 39 of volume II, "with posterior infarction there is a tendency for the T-waves to become lower and inverted in lead I and positive in lead III," were really acceptable to the advisory and review panel of 28 distinguished authorities. The publication deserves the highest commendation for the excellence and clearness of the reproductions of electrocardiograms and the simplicity and conciseness of the accompanying text that make these volumes most valuable to anyone concerned with learning or teaching clinical electrocardiography.

Studies in Topectomy. Edited by Nolan D. C. Lewis, M.D., Carney Landis, Ph.D., D.Sc., and H. E. King, Ph.D. Cloth. $6.75. Pp. 248, with illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16; 99 Great Russell St., London, W.C.1, England, 1956.

The New York Associates in Brain Research explored in 1948 to 1949 the potentialities of psychosurgical methods as a therapy for mental disorder. They used topectomy of the frontal lobes on 66 patients, many of whom were chosen for the severity of their mental disorder. The operations, both frontal ablations, performed bilaterally, were of two types, one removing the superior portion and the other the more orbital section of the lobe. There was no operative mortality or lasting neurological changes. Psychiatric evaluation was undertaken about two years after the operation. The results were not impressive. The procedure was considered of limited value for chronic schizophrenics but of slight usefulness for chronic psychoneurotics and for some of the patients with manic-depressive reactions and with involutional psychoses. An independent psychiatric evaluation by another group of investigators was even less enthusiastic, and concluded from the strictly therapeutic viewpoint that the verdict at best would have to be "not proved." In general the importance of applying therapeutic measures, even topectomy, before the psychotic process has become fixed, was emphasized. The study was carefully planned and executed by a skilled research team. The report reflects their high standards and excellent tallying of the results. The details of the surgical technique, psychometric studies, vestibular function test, and other investigative methods are reported fully and clearly. Although it is published five years after the end of the project, the book is a valuable contribution to our knowledge of topectomy and its effect on psychiatric disease.

Textbook of Gynecology. By Emil Novak, A.B., M.D., D.Sc., Gynecologist-in-chief, Bon Secours Hospital, Baltimore, and Edmund R. Novak, A.B., M.D., F.A.C.S., Instructor in Gynecology, Johns Hopkins Medical School, Baltimore. Fifth edition. Cloth. $11. Pp. 840, with 543 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2,

This popular book did not need much revision to bring it up to date. The few important contributions to gynecology made in the last four years are included. The chapter on uterine cancer was entirely rewritten because of the controversy concerning carcinoma in situ. Likewise, the chapter on pelvic tuberculosis was completely rewritten because of advances in both diagnosis and treatment of the disease. The authors mention the new skin biopsy tests for sex determination. They consider kraurosis and leukoplakia of the vulva together because of the frequency with which the two terms are wrongly applied and the existing confusion as to their differentiation. The authors do, however, make a rational distinction between the two conditions. There is a full description of carcinoma in situ, with emphasis on the difficulties in diagnosis. The authors again summarize the important essentials of the responsibilities of the general practitioner in the campaign against cervical cancer. In the chapter on tuberculosis of the generative organs, the place of streptomycin, aminosalicylic acid, and derivatives of isonicotinic acid is discussed. There is no doubt that the Novaks have again produced a classic book that should continue to be profitably studied throughout the world.

QUERIES AND MINOR NOTES

FETAL EFFECTS OF DEMEROL ANTE PARTUM

To the Editor:—*In the local hospital the use and dosage of Demerol in a woman in labor with an intrauterine pregnancy was questioned when an infant had a four-or-five minute delay in cry and respiration attempts. A review of the available literature reveals that it is the consensus that Demerol will not have a depressant effect on any infant, whether at term or premature. The mother had received a total of 200 mg. of Demerol within a three-hour period prior to the actual delivery. The last dose was 100 mg. and was given 20 minutes prior to delivery. How soon after injection can one normally expect a peak of effect in the infant (if any)? What is the maximum dose that could safely be given to a normal mother weighing 70 kg. (154.2 lb.) in labor without danger of depression to the baby? Is there any place in the literature indicating that morphine (given to the mother in labor) was not depressant to the baby?* *M.D., Wis.*

Answer.—The depressant effect of Demerol on the fetus depends on certain variables that cannot be predicted in any given case. These variables include the tolerance of the mother, her weight, the rapidity of absorption from the injection site, and the type of anesthesia used for delivery. In general, the maximum effect of an intramuscular injection should occur about one hour after administration to the mother. This is rarely of clinical significance if conduction or local anesthesia is used. With general anesthesia, with cyclopropane or nitrous oxide ether, the narcotizing effect of this combination of drugs may be of significance to the baby. Most normal labors, of 6 to 10 hours' duration, can be readily managed with a single dose of 100 mg. of Demerol, preferably combined with scopolamine (hyoscine) in a dose of 0.4 mg. If this is inadequate to control the patient's discomfort, trichloroethylene (Trilene) inhalation or the judicious use of chlorpromazine or one of its derivatives is considered preferable to the repeated doses of Demerol. When repeated doses of narcotics of any type must be given for the control of pain in labor, when they are used at repeated irregular intervals for the purpose of obtaining rest in a prolonged labor, or when the mother shows a profound response to these drugs, their narcotizing effect upon the baby may be effectively and promptly minimized by the administration of amphetamine or nalorphine (Nalline) hydrochloride to the mother approximately 15 to 30 minutes prior to delivery. Morphine sulfate has been shown both clinically and experimentally to be a depressant to the baby. This consultant is unaware of any valid data to the contrary.

PREMATURE GRAY HAIR

To the Editor:—*In the May 19 issue of* The Journal, *page 299, is a query on graying of hair. Is there any known medication or treatment that will forestall or delay premature graying of hair? If not, what is a safe method for use in changing the color of the hair to its former color?* *M.D., South Carolina.*

Answer.—There is no known medication or treatment that will forestall or delay premature graying of the hair. Reports of the effectiveness of pantothenic acid or p-aminobenzoic acid in delaying or lessening premature graying of the hair have never been proved. As far as a safe method of changing the color of the hair is concerned, there is no absolutely safe procedure. An occasional person will still react unfavorably to the methods mentioned subsequently. The metallic hair dyes are successful only when frequent applications are made, and the desired color may appear after a series of treatments that progressively darken the hair. The usual solutions contain silver, copper, iron, or lead, which act with the sulfur content of the hair to deposit a metallic sulfide on the shaft. Silver nitrate, in combination with a 1% solution of pyrogallic acid as a reducing agent, may be adopted for all shades from white or brown to black, depending on its strength. The synthetic organic dyes are also effective and are of two types. The first, or "azo" type, has a low index of sensitivity but has the disadvantage that several applications are necessary to obtain the desired shade. The most popular types of dyes are those of the amine or aniline type. They have two characteristics that render them superior to their predecessor: First, the desired color is usually acquired at one sitting. Second, the colors themselves offer a wide range of choice and are much more natural in appearance. Several preparations are on the market, and patch tests should be performed prior to their usage. This synthetic dye is usually sold in two bottles, of which one contains a 1 to 3% aqueous solution of the para dye and the second an oxidizer such as hydrogen peroxide or sodium persulfate or perborate. Some of these are available for home application, although it is usually preferable to have the applications made by a professional. Inasmuch as the chemicals employed are not easily handled by the amateur, the skill and experience of a careful operator should minimize the possibility of untoward side-effects.

ULTRAVIOLET BLOOD IRRADIATION

To the Editor:—*A 39-year-old man is being treated for "a general run-down condition." Apparently he is not progressing as well as anticipated. His brother has chronic bilateral thrombophlebitis of both legs and, in addition to saphenous vein ligations and anticoagulant therapy, he has received ultraviolet blood irradiation, possibly according to the Knott technique. It is stated that some improvement has followed this therapy. The treating physician for the first-mentioned man feels that ultraviolet blood irradiations may be of value in improving his patient's condition. I would appreciate an opinion on the efficacy of ultraviolet blood irradiation in regard to its application to the broad category of "general run-down condition."*

M.D., Massachusetts.

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—There is no objective evidence that ultraviolet irradiation of the blood by the Knott technique has any beneficial effects. It has been used widely for a great number of conditions, with purportedly uniform good results. The nature of the ultraviolet treatments is such that a great deal of psychotherapeutic benefit may ensue from their use. This, together with the enthusiasm of those who have used the treatments, probably accounts for the reported value of the technique. Its use for any patient with a "general run-down condition" is not indicated. It is essential to establish why a 39-year-old man is "run-down," so that rational therapy may be instituted.

Answer.—Ultraviolet blood irradiation enjoyed a brief display in the medical literature from 10 to 15 years ago. A portion of blood (about 250 cc.) was removed from a patient, citrated, and then, after exposure to powerful ultraviolet irradiation in a suitable irradiating chamber, was immediately pumped back into the venous system. While the claims of the favorable effects of hemoirradiation on bacterial infections did not violate credibility, in view of the known bactericidal potency of ultraviolet rays under suitable conditions, reports soon appeared suggesting the efficacy of hemoirradiation in acute thrombophlebitis, bronchial asthma (intrinsic), rheumatoid arthritis, osteoarthritis, postfebrile poliomyelitis, "non-healing" wounds (apparently due to chronic osteomyelitis or vascular insufficiency), and paralytic ileus. As a result of the alleged dramatic response of chronic as well as acute diseases, a hypothesis of "ultraviolet ray metabolism" was developed.

As often occurs in medicine, a reputedly successful, if not dramatic, new therapy in the hands of a few is quickly taken up by the many and applied to a wide array of conditions of

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

unknown etiology in the hope of a cure. Hemoirradiation was no exception, and disappointment followed inevitably. More important, it stimulated well-controlled experiments in which bloods seeded with various pathogens were irradiated. These failed to corroborate the clinical reports. Indeed, in saline medium, where ultraviolet could be expected to reach the bacteria in more potent doses because of minimal absorption, irradiation also failed to eliminate the organisms. In nonbacterial diseases it was never proved that ultraviolet irradiation had an "energizing" effect on the body, and no satisfactory short-term or long follow-up proof on chronic arthritides and other conditions were published. The whole concept of this form of treatment, in fact, was never subjected to a well-controlled analysis free from objectionable methodology. Uncritical empiricism based on a tenuous and untested hypothesis may briefly lead to the unbridled use of an agent, even for such vague conditions as "general run-down condition." Today, ultraviolet hemoirradiation is a medical curiosity that did not fulfill the therapeutic claims originally made for it.

CAUSE OF DEATH

To THE EDITOR:—*In "Collectivism on the Campus: The Battle for the Mind in American Colleges," by E. Merrill Root (New York, the Devin-Adair Co., 1955, p. 133), is a passage dealing with the death under mysterious circumstances of a young student in California. After an autopsy, the cause of death was given as inhibition. This matter was not discussed at length, but apparently it referred to such stimulation of the central nervous system by terror that nervous reflexes stopped the action of the heart and/or lungs. I would appreciate it if you would comment on this diagnosis.*

Thomas Parker, M.D., Greenville, S. C.

This inquiry was referred to two consultants, whose respective replies follow.—ED.

ANSWER.—There are many instances in fiction and occasional, but unverified, references in scientific literature to sudden death during a period of extreme emotional stress. One might postulate, although it is extremely improbable, that sudden hypothalamic overactivity, in response to fear or some other emotion, might cause vagal stimulation to such a degree that it would bring about cardiac arrest and/or inhibition of respirations. This, however, has never been demonstrated or proved. One might question whether such a phenomenon, if it exists, could be related to the so-called acute brain death, which sometimes occurs without warning in schizophrenia and other so-called functional mental diseases. In this, however, there is usually a brief period of of extreme hyperpyrexia, motor hyperactivity, and either stupor or convulsions preceding death. In these cases, furthermore, extensive cellular alterations in the brain have been reported. Before answering this query, the original reference was reviewed. When the body of the subject was found, it was lying in a furnace pit near an unconnected gas heater. The gas that fed the furnaces was turned off, and the furnace room door was standing open. A few days later, as soon as an investigation began, the entire basement was flooded, and other possible clues were obliterated; apparently the flooding was purposely done. The only finding in the autopsy was pulmonary edema.

It is apparent, from the circumstances leading to death and the findings after death, as well as from lack of any proof of inhibition of purely psychic origin and not secondary to toxic or other organic stimulation of centers that depress cardiac and respiratory functions, that one must conclude that in this case the cause of death was not found. One must assume that external causes of toxic or other origin, which were not brought to light in what was apparently a very complete autopsy, were responsible for the death of the subject. It was the final conclusion that this was "death by homicide" (page 137). While inhibition may be a theoretical cause of death, it is not so accepted clinically. It would be better in cases like this to conclude, as was done in this case, that death was due to external causes. One should be willing to admit that the cause was not found and should not rely on intangible, unscientific explanations.

ANSWER.—The Standard Nomenclature of Diseases and Operations published by the American Medical Association does not list "inhibition" as a disease entity. Inhibition as a cause of death is not acceptable in medical circles and probably would not be accepted by boards of health on a death certificate. Many deaths occur under mysterious circumstances, and the cause in any one can be overlooked in an autopsy unless the examination covers all phases necessary to accomplish this.

TACHYCARDIA

To THE EDITOR:—*A 75-year-old woman suffers from chronic suppurative bronchitis and asthma and is highly allergic to egg albumin. She has frequent attacks of tachycardia, which usually occur after dinner and may last half an hour. During the attack the pulse is about 120 per minute, full and tense, and there is shortness of breath and at times pain extending down the arms. Is there any therapeutic measure that might reduce the frequency of these attacks or give relief?*

M.D., New Jersey.

ANSWER.—It would be helpful to have more information concerning the nature of the tachycardia and the characteristics of the rate and rhythm. If there is any irregularity of the rhythm, then one must consider the possibility of a paroxysmal fibrillation or an atrial flutter with varying block. An electrocardiogram taken during an attack would help to settle this question.

If the rate is perfectly regular at 120 beats per minute, then the underlying mechanism is probably a normal sinus rhythm. Therefore, one must suspect that the underlying cause is coronary insufficiency, probably induced by the demands of digesting a heavy meal. Reducing the amount of food at the evening meal and dividing the total daily amount of food into four or five small meals may be helpful. Administration of glyceryl trinitrate (nitroglycerin), 1/200 grain (0.3 mg.) sublingually, may be tried at the onset of her attack. If the glyceryl trinitrate aborts the attack and relieves the dyspnea and pain, then the usual program for angina should be instituted. If it can be demonstrated that the attack is a paroxysmal type of fibrillation or atrial flutter with varying block, then administration of quinidine sulfate, 200 mg. after meals and at bedtime, is indicated in an effort to prevent the attacks. An additional 200-mg. tablet may be given during the attack. In spite of the highly allergic background of the patient. it is doubtful that any allergic reaction is playing a role in the attacks.

AZOOSPERMIA

To THE EDITOR:—*Examination of a 34-year-old man was essentially negative apart from slight obesity. Urinalysis and serology were negative. A fertility investigation by a urologist revealed azoospermia. The patient asks: "I was working with a poison gas unit during the war—could this have caused me to be sterile?"* *Thomas W. Parkinson, M.D., Gastonia, N. C.*

ANSWER.—The germinal epithelium of the testes may be severely damaged as a result of repeated absorption of small doses of toxic substances over a long period of time through the skin, lungs, or alimentary tract. Alcohol and morphine are known to act in this way. Various industrial poisons have been inculpated in the same respect, among them lead, mercury, sulfocarbonate, benzene (benzol), toluene (toluol), phosphorus, and turpentine. This consultant has no information about the chemistry of the gases used in warfare or about the precautions taken to protect men working with them. There would seem to be at least a theoretical possibility that the spermatogenic apparatus might be exposed to injury. Further investigation is needed to throw light on the cause of azoospermia in this patient. Testicular biopsy may show normal spermatogenesis, and in that event the trouble is obviously a blockade in the duct system; it may reveal aplasia or hypoplasia of the seminiferous tubules; it may show germinal epithelium that is histologically fairly normal but functionally inactive, and if at the same time hormone assays demonstrate a low level of gonadotropins the diagnosis of pituitary eunuchoidism is apparent. In all of the foregoing cases the primary cause of azoospermia would be adequately explained by the findings and is clearly unrelated to any sort of chronic intoxication. However, if the biopsy finding is sclerosing tubular degeneration and atrophy, one may consider the possibility that a toxic factor was initially responsible, though this is by no means proved by the evidence obtained.

BRONCHIAL ASTHMA WITH TUBERCULOSIS

TO THE EDITOR:—*How frequently does bronchial asthma occur with pulmonary tuberculosis? A number of patients in all the different stages of pulmonary tuberculosis have all the classic signs of bronchial asthma. Are the physical signs and symptoms due to bronchial asthma, per se, or are they the result of intermittent flaring up of the tuberculous process? During these episodes these patients have been given the usual treatment for bronchial asthma and this has relieved them. Is there some other treatment? Is this an allergic manifestation to the tubercle bacilli?*

M.D., Philippines.

ANSWER.—The incidence of bronchial asthma in patients with pulmonary tuberculosis is identical with its incidence in the general population. This represents true allergic bronchial asthma, with the sensitivity being due to the common antigens, and does not represent an allergic manifestation to the tubercle bacilli. The conventional treatment for asthma is indicated and should produce results uniform with those obtained in nontuberculous patients. The only exception to this statement is that steroid therapy should not be used in those patients having known tuberculosis or in those suspected of having tuberculosis. It is also true that the physical signs and symptoms of bronchial asthma may occur in patients with pulmonary tuberculosis and be due to the tuberculosis and not to allergic bronchial asthma. In these patients, the common cause for these findings is due to involvement of the bronchus by either a tuberculous bronchitis and/or pressure on the bronchus by an enlarged mediastinal lymph gland. These patients will also show a response to the conventional therapy with bronchodilator drugs, but this response will be only temporary and symptomatic and therefore this therapy must be accompanied by therapy with antimicrobial drugs.

DRUG ADDICTION

TO THE EDITOR:—*A 45-year-old male patient with osteoarthritis takes the following amounts of medication nightly in order to obtain satisfactory rest: codeine, ½ to 1 grain (30 to 60 mg.); three to four Bufferin tablets; and one or two Valmid tablets. Is there any danger of addiction or other harm from continued use of the above?* *M.D., New Hampshire.*

ANSWER.—The danger of addiction in the case described depends primarily on the personality structure of the patient. If he is a mature, emotionally stable individual, the danger of addiction would be remote. On the other hand, if he is an unstable person there would be some danger of addiction to codeine. Indications that addiction might be developing would be requests for increase in amounts of codeine or attempts to obtain supplies without obtaining new prescriptions and by obtaining prescriptions from more than one physician. This danger, which is slight, is further minimized if close contact with the patient and with his family can be maintained. There should be no harm from continued use of either the codeine or Bufferin. Sufficient information concerning idiosyncrasies to Valmid is not available to evaluate the danger of long-continued use of this particular substance. If the patient can be examined at frequent intervals, any untoward drug intoxication should be detected before significant harm is done.

TRAUMATIC AMPUTATION OF FINGER TIP

TO THE EDITOR:—*What would be an approved method for immediate definitive treatment of a 35-year-old aircraft factory worker whose injury consisted of an almost complete guillotine type of crushing amputation, bone and soft parts, of the right index finger, through the base of the distal phalanx, involving the distal joint? There remained only a slight subcutaneous bridge attaching the amputated end to the balance of the digit? All major digital vessels apparently had been severed, as there was no bleeding from the distal stump, while the proximal end bled freely.* *M.D., California.*

ANSWER.—Replacement of the tip of the finger would, in all probability, not be successful, as the bulk of the tissue was too great and the injury was a crushing one. If the skin of the pulp was not too crushed, all the subcutaneous fat could be removed and the skin of the pulp laid across the end of the stump. Usual procedures in such a case would be to cover the end of the stump with a free skin graft or to transfer a flap to it from the thenar eminence. The objection to the latter is that in a 35-year-old man the joints would stiffen in the three weeks that the flap is attached. Perhaps the best way would be to use a cross-finger flap from the dorsum of the long finger and skin graft the donor site. Another possibility would be to raise an immediate pedicle flap from the abdomen and place it over the end of the finger. Such a procedure is usually left for a secondary operation, if it proves to be necessary. If bone is projecting, it should be trimmed off, and, if a joint surface is presenting, it should be denuded of cartilage.

TREATMENT OF PEDUNCULATED POLYPS

TO THE EDITOR:—*Two polyps were excised recently from a 55-year-old male. The polyps were attached to the sigmoid flexure by a stalk about 2 in. in length. The microscopic report revealed that the stalk portion of the glandular mucosa is not unusual. A portion of the distal part of the polyp showed hyperchromatism of some of the irregular glandular acini. Heaping up of the glandular epithelium was seen at this portion, with component cells exhibiting moderate variation in size and shape. Mitotic figures are fairly frequent in this area. The diagnosis was malignant adenomatous polyp. At operation the polyp was excised at the base of the stalk. Is any further surgery indicated at present?*

M.D., New York.

ANSWER.—Review of the experience at a large cancer center where several thousand pedunculated, adenomatous polyps have been removed showed there has been no instance of lymph node metastases when cancerous changes have been superimposed upon the periphery of the polyp. It would seem, therefore, that the 55-year-old patient having two pedunculated polyps has been adequately treated and that future emphasis should be directed at the detection of other polyps, which are quite likely to develop in other areas of the same lower intestine. Pedunculated carcinomas and sessile polyps, containing foci of adenocarcinoma, on the other hand, have been seen to metastasize to the regional lymph nodes and must be treated radically from the onset as infiltrating carcinoma.

BRANCHIOGENIC CYST

TO THE EDITOR:—*What would be the recommended treatment of a healthy 14-year-old girl with a now quiescent congenital cyst (and/or fistula), branchiogenic, in the lateral cervical region, which has twice previously necessitated incision for local abscess formation?* *M.D., California.*

ANSWER.—A branchiogenic cyst with recurrent fistulous communication is a distinct indication for a complete and adequate excision of the cyst. Incision alone would of course only allow repeated recurrent draining abscess formation, and the actual cyst itself must be removed totally by meticulous and careful surgery.

DIABETIC NEUROPATHY WITH INCONTINENCE

TO THE EDITOR:—*What is the treatment for diabetic neuropathy of the legs with incontinence of the bladder and rectum? Are steroids of any value?* *M.D., New Jersey.*

ANSWER.—The treatment of diabetic neuropathy with incontinence of the sphincters is very unsatisfactory. Some improvement has been noted after intensive treatment with crude liver extracts given intramuscularly (3 cc. daily) and large doses of vitamin B_{12}, of the order of 1,000 mcg. per day. The steroids are probably of no help.

EXERCISE AND THE DIGITALIZED HEART

TO THE EDITOR:—*How does exercise affect the rate of the completely digitalized heart?* *M.D., Missouri.*

ANSWER.—Exercise produces less acceleration of the heart that has been digitalized. This is best seen in auricular fibrillation. The amount of this effect depends on the dose of digitalis. The more complete the digitalization, the less the acceleration of the heart with exercise.

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THE MEDICARE PROGRAM

The Office for Dependents Medical Care has issued additional information designed to answer questions arising from the armed forces new and broadened program of medical care for service families. The program became effective Dec. 7. In a letter to state medical societies and groups serving as fiscal agents for provision of care by private physicians, Major. Gen. Paul Robinson, director of the office, stresses the "medicare" program is one of full service coverage. He makes these points: 1. It is intended that medicare as authorized by the last Congress will be on a basis comparable to that provided in uniformed medical facilities. Except for specified amounts to be paid by the patient, services provided under the law will be paid for in full from the government in accordance with published schedule of allowances. "In most instances, this means that the physician participating in the program will receive payment for his usual charge or the amount established in the local schedule of allowances, whichever is less," the letter states.

2. There may be unusual instances in which the physician will believe that an allowance greater than that prescribed in the local schedule is justified. "In such cases, the physician should look to the government for additional payment and not to the patient." Provision is made for the doctor to submit a special report to his state medical society and in turn to the government as request for added payment, and such payment will be made upon approval by the medical society's review board and the government contracting officer.

The Office for Dependents Medical Care also points out that it is not contemplated that the government will authorize payment for drugs, medicinals, or other medical supplies except those furnished to an inpatient while hospitalized or those administered directly by a physician in his office.

On the question of identification of military dependents, the office says that doctors may accept as evidence the post exchange card issued to dependents, the combined post exchange–commissary–military medical care card, also the military dependent identification card. After July 1 of next year, a new Defense Department identification card for medicare alone will be the only card honored for this purpose.

FEDERAL WORKERS HEALTH INSURANCE

A fresh try at drafting legislation that will provide both basic and major medical expense coverage for federal employees is being made by the Civil Service Commission. Despite repeated failures at getting a bill suitable to all parties passed in Congress, administration officials are optimistic over prospects in the 85th Congress convening Jan. 3.

The administration's 1956 proposal, which would have provided for catastrophic illness coverage with the government paying the premiums, came up against opposition from some nonprofit plans and labor spokesmen. Accordingly, no bill passed this year. The Civil Service Commission the year before was unable to get an agreement on a basic coverage plan. The new approach is to tie both programs into one bill that will satisfy federal employees unions, commercial carriers, and Blue Cross and Blue Shield.

One of the large federal workers unions, the American Federation of Government Employees, has suggested a combined program that would permit the employee to take out group health insurance with any type of carrier that met commission criteria for soundness of operation. The government and the worker would share equally in payment of premiums, which would be handled through payroll deduction.

THE DOCTOR-DRAFT FOR FEBRUARY

A total of 450 physicians are scheduled to be called in February under the doctor-draft, with 250 men sought by the Army and 200 for the Air Force. The six-year-old doctor-draft act expires next June 30, and the Defense Department has said it has no plans for asking Congress for another extension. The Selective Service headquarters, meanwhile, has instructed local draft boards to review immediately the essentiality or availability of young priority 3 physicians serving residencies. Comments the Selective Service: "In this connection we would like to point out that there are a number of younger priority 3 men in residency training who are not essential but are so classified. We are informed that some of them have been deferred as necessary to the operation of the hospitals."

The agency defined "young" as men up to the age of 37. It said that "it is hoped that there is yet times to get a sufficient number of younger men reclassified into class 1-A to satisfy these proposed calls without going into the upper age bracket."

In making their reports of availability of doctors for the February call, boards will exclude physicians who will be 35 years of age or older on Feb. 27, 1957, and who have applied at any time for a commission in the armed forces in a medical, dental, or allied specialist category and have been rejected solely because of physical disqualification.

From the Washington Office of the American Medical Association.

PROGRAM TO INCREASE RESEARCH MANPOWER

Starting a new federal program designed to increase manpower for research in basic medical sciences, the National Institutes of Health announces award of 44 five-year fellowships to scientists in universities and medical schools. Recipients are scientists with a doctor's degree in biochemistry, pharmacology, physiology, microbiology, pathology, and the psychological sciences.

Each award calls for a salary not in excess of $10,000 per year, plus up to $2,000 for part of the expense of research. The institution sets the salary level at approximately that of scientists doing similar research and teaching as members of the regular faculty. While the fellows continue their research, sponsoring institutions will assign them appropriate teaching responsibilities so they may qualify for full-time academic positions at higher levels.

Inauguration of the program was preceded by more than two years of study by the Public Health Service, aided by a group of outside experts and deans of medical schools and heads of university departments involved in medical research. In explaining why the program is needed, PHS Surgeon General Burney said that this year more than 200 research positions are open on the faculties of medical and basic science fields, including 55 professorships, 52 associate professorships, and 79 assistant professorships.

The plan is to award between 40 and 50 fellowships annually until 250 have been set up by the fifth year. Thereafter the program will be maintained at this level "until the national deficiencies have been met." This year, fellowships will cost about half a million dollars.

Four institutions—University of California, Harvard, University of North Carolina, and Canada's Albert Einstein College of Medicine—received three fellowships each. Other schools receiving one or two scholarships are Yale, Georgetown, University of Florida, Emory, University of Kansas, Tulane, Johns Hopkins, Michigan, Minnesota, Washington University, New York University, Albany School of Medicine, Rochester, Bowman Gray School of Medicine, Duke, Wake Forest, Western Reserve, Ohio State, Oklahoma, Pennsylvania, Pittsburgh, Tennessee, Vanderbilt, Baylor University, University of Washington, and Marquette.

MALARIA ERADICATION PROGRAM

The hemisphere-wide malaria eradication program is gaining momentum, and integrated programs of various governments leave no doubt as to the eventual success of the campaign. That is the latest word from the Pan American Sanitary Bureau, which cites some examples: 1. Some 3 million houses in malarious areas of Mexico will be sprayed starting Jan. 1, the largest undertaking of its kind ever attempted in this hemisphere. The United Nations Children's Fund is providing large supplies of insecticides, trucks, and other essential materials, but with the Mexican government furnishing most of the funds and direction.

2. Of the 20 countries originally infected by malaria, 2 (the United States and Chile) have completed eradication; 10 others in addition to Mexico have begun eradication (Argentina, Brazil, Ecuador, El Salvador, Guatemala, Haiti, Honduras, Dominican Republic, and Venezuela); 3 have completed plans for converting control programs to eradication programs (Nicaragua, Panama, and Paraguay); and 5 are either surveying or considering conversion to eradication campaigns (Bolivia, Colombia, Costa Rica, Cuba, and Peru).

The Bureau has set up a coordinating office for malaria eradication in Mexico City to advise and guide programs under way or in preparation in various countries.

NEW AIR FORCE MEDICAL CENTER

The Air Force is scheduled to award the first contract this month for the construction of an $8,800,000 Aero Medical Center that will house the Air Force School of Aviation Medicine. It will be built at Brooks Air Force Base, San Antonio, Texas, and is slated for completion at the end of 1958. The work of the school is now carried on between Randolph Air Force Base, Texas, and Gunter Air Force Base, Ala.

Comments the Air Force: "Establishment of this single aeromedical center will allow the Air Force to conduct more extensive research into the medical aspects of supersonic flight problems, and to provide greater aviation medicine teaching facilities than are now available. Emphasis will be placed on developing means of protecting fliers at the high speeds and altitudes which are now encountered, or expected to be, in the future." The center was authorized by the 82nd Congress in a fiscal 1953 military construction program bill.

MISCELLANY

The Federal Civil Defense Administration's health office had a special exhibit at the American Public Health Association convention depicting physical characteristics of radiological fall-out, hazards of fall-out, and suggested protective measures. . . . Dr. Harry Davis Bruner is the new chief of the medical branch of the Atomic Energy Commission's division of biology and medicine. . . . The Walter Reed Army Institute of Research has developed a vaccine that is said to effect a 98% reduction in acute respiratory illnesses caused by adenoviruses. As the vaccine has been tested only with military personnel, its effect on a large section of the population is not known. . . . Forty participants have completed the three-week 13th Interagency Institute for Federal Hospital Administrators. . . . When the first plane load of Hungarian refugees landed in the United States the first person they saw was Dr. Isidor Abrahamer of the Public Health Service, who is himself a refugee. Dr. Abrahamer, who is assigned to the foreign quarantine service, is responsible for the medical examinations of the Hungarian refugees. . . . Mrs. H. Chapman Rose of Cleveland has been appointed a member of the National Advisory Mental Health Council, which advises the activities of the National Institute of Mental Health. . . . Col. Frank M. Townsend, U. S. A. F., Deputy Director of the Armed Forces Institute of Pathology, has been elected chairman of the Joint Committee on Aviation Pathology of the Department of Defense.

THE JOURNAL

of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 162, NO. 15 | CHICAGO, ILLINOIS | DECEMBER 8, 1956

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SURGICAL RENAL LESIONS ASSOCIATED WITH PREGNANCY

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• *Hormonal factors that control the course of pregnancy as well as the pressure of the gravid uterus on the ureters cause physiological changes in the kidneys and ureters of at least 90% of pregnant women. Mechanical pressure occurs only at the pelvic brim, but the hormonal influences producing dilatation, atony, and reduced irritability of smooth muscle involve the entire upper urinary tract. Previous diagnosis of urinary disease or congenital anomalies is important in anticipating these changes. Pyelonephritis is still frequent, but its management in pregnant women is no longer different from that in the nonpregnant. Preexisting surgical renal disease must be carefully evaluated before pregnancy is permitted; disease discovered during pregnancy may or may not necessitate therapeutic abortion. The decision in either case depends on the nature and extent of the renal disease, the general health of the patient, and, in borderline cases, the risks that the parents are prepared to take in order to obtain a child.*

With the possible exception of the cardiovascular system, the genitourinary tract is probably the organ system of the body most vulnerable to complications of pregnancy. In Folger's[1] experience, of all women hospitalized at Western Reserve for treatment of complications of pregnancy, the largest group had involvement of the urinary tract. It is therefore of the utmost importance, to both obstetricians and urologists, not only to review the management of surgical renal lesions discovered during pregnancy but also to evaluate properly the changes that can be expected to occur in the upper urinary tract during pregnancy and their significance with regard to preexisting surgical renal disease.

Physiological Changes in Ureters and Kidneys

The physiological changes occurring in the upper urinary tract during pregnancy have been recognized since 1843, when they were first described by Cruveilhier.[2] These changes consist in dilatation of the upper two-thirds of the upper urinary tract, with impairment of drainage and resultant stasis of urine and back-pressure in the renal pelves. It is now generally agreed that these changes are the result of hormonal alterations as well as of mechanical factors incident to pregnancy. However, the hormonal influence is of greater importance, since it has been shown that such changes can be reproduced in the nonpregnant woman by administration of progesterone and also that they tend to lessen toward the end of pregnancy as the hormonal balance changes in the circulating blood.[3] Van Wagenen and Jenkins[4] were able to show that after spontaneous death and absorption of a fetus or surgical removal of a fetus, if the placenta remains in place and active, the changes in the upper urinary tract remain. It is also well known that certain of these changes occur during the first trimester of pregnancy, before there is sufficient enlargement of the uterus to result in any real mechanical obstruction. Because of the common embryologic origin of the uterus and upper urinary tract collecting system, the basic hormonal influence intended primarily to produce dilatation, atony, relaxation, softening, and reduced irritability of muscle response of the uterus in the normal course of pregnancy inevitably has the same effect on the ureters and renal pelves.

That mechanical factors also play a part is evidenced by the fact that the changes end where the ureters cross the pelvic brim. This can be explained by the pressure of the uterus on the ureters at that point. The changes are more pronounced on the right because of the dextrorotation of the uterus, the prominence of the right iliac artery, and the cushioning effect of the sigmoid colon on the left. These changes appear grossly as elongation and tortuosity of the ureters and dilatation of the ureters and renal pelves.[5] The microscopic appearance is characterized by hyperplasia and hypertrophy of the smooth muscle and connective tissue,

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Read before the Joint Meeting of the Section on Obstetrics and Gynecology and the Section on Urology at the 105th Annual Meeting of the American Medical Association, Chicago, June, 14, 1956.

with infiltration by lymphocytes, plasma cells, and leukocytes, and increased vascularity and edema. Physiologically, the irritability response of the smooth muscle of the ureter to stimuli is reduced. These changes become gradually more pronounced up to the seventh month of pregnancy and diminish during the eighth and ninth months. The upper urinary tract usually returns to normal by the end of the third postpartum month, although in some instances the upper ureters and renal pelves, particularly on the right, may become permanently dilated after multiple pregnancies.

Certain degrees of dilatation of the upper urinary tract may also occur as a result of large abdominal masses other than a pregnant uterus, owing entirely to the mechanical factors discussed in the preceding paragraph, but this is not nearly as pronounced or consistent as in pregnancy. At present, therefore, it seems safe to assume that the anatomic and functional changes that take place in the ureters and kidneys are due largely to the same substance that controls the course of pregnancy in the uterus. Attempts to identify this substance accurately have not so far been successful.

Pyelonephritis of Pregnancy

The fact that these physiological changes occur in at least 90% of pregnant women easily explains the increased disposition of these women to infection of the upper urinary tract. Infection has been variously reported as occurring up to six times more often in pregnant than in nonpregnant women. However, although pyelonephritis of pregnancy was formerly a serious problem, sometimes becoming of surgical importance, with the modern advances in chemotherapy of urinary infection, its management is no longer different from that in nonpregnant women. Today such patients rarely require hospitalization and still more rarely require indwelling ureteral catheter drainage to control the infection. A striking contrast to this fact is the report of Crabtree and Prather[6] in 1930. At the Boston Lying-in Hospital, between 1916 and 1922, before the days of modern chemotherapy, they noted that, of 46 hospitalized women with pyelonephritis of pregnancy, only 17 became afebrile and were allowed to complete the pregnancy. Pregnancy was interrupted or spontaneous abortion occurred prematurely in 25 patients. Six infants died, and, although there were no maternal deaths in the hospital, three mothers died at home some months later from the effects of renal infection. In reviewing the hospital records at Western Reserve, Folger[1] also showed that, in the 10-year period ending in 1943, of 12,981 pregnant women, 372 (2.9%) were admitted to the hospital because of pyelonephritis. In the succeeding 10 years, of 17,556 pregnant women, only 106 (0.6%) required hospitalization for the same reason.

Obviously, therefore, although the underlying factor of retarded drainage of urine with resulting stasis in the kidneys still causes the same predisposition to infection of the upper urinary tract in pregnancy as it always has, these cases are now rarely of surgical importance, with the exception of those few instances in which preexisting anatomic defects interfere with drainage. In such instances surgical intervention or interruption of the pregnancy may become necessary because of inability of chemotherapy alone to control the infection. The affected kidney can often be surgically drained either by indwelling ureteral catheter or by introduction of a nephrostomy tube, without necessarily removing the kidney or interrupting the pregnancy. During the puerperium the kidney may be reevaluated and removed if found to be destroyed or else the original defect plastically repaired if indicated.

Congenital Anomalies of Upper Urinary Tract

Congenital anomalies of form and position of the upper urinary tract may be well tolerated during pregnancy, in the absence of infection, and often remain undiagnosed. However, if the physiological changes of pregnancy are superimposed on pathological changes already present, there is an increased predisposition to dilatation of the renal pelves, impairment of function and drainage of urine, and infection. This is true of renal ectopia, fused kidneys, polycystic kidneys, congenital obstructions of any part of the upper urinary tract, vascular anomalies producing obstruction, certain cases of malrotation and malposition of the kidneys, and congenital renal ptosis. In some instances, however, ptosis may be temporarily improved during pregnancy, owing to the supportive effect of the enlarged uterus. Therefore, in all women known to have such anomalies the competency of both kidneys should be carefully evaluated before pregnancy is advised.

Renal Ectopia.—Renal ectopia is of particular importance, because of the potential danger of the traumatic effect of normal labor to such kidneys. Because of their abnormal form and position, more often than not, prior to pregnancy, such kidneys exhibit varying degrees of hydronephrosis, infection, and impairment of function. Reviews of the world's literature on this subject by Tweed[7] and by Anderson and associates[8] show that ectopic pelvic kidneys have been reported as occurring approximately once in every 4,000 pregnant women, although many asymptomatic ones undoubtedly remain unrecognized. Of 113 cases discussed by Tweed[7] of pelvic kidneys recognized during pregnancy, 80% were unilateral, 7 solitary, and the remainder bilateral with or without fusion; of the unilateral cases, 79% occurred on the left side. One-half of these were recognized during pregnancy and the remainder either during the postpartum period or at autopsy. There were 226 pregnancies in these women; the incidence of abortion was 15.4%, the total fetal mortality rate 16.7%, and the total maternal mortality rate 10.2%. However, there have been no maternal deaths since 1927. Delivery was spontaneous in 73% of these women, by cesarean section in 17%, and by forceps in 6. Downs and Burns[9] reported that, of seven women having solitary pelvic kidneys, three (42.8%) died of renal failure as a result of pregnancy and spontaneous delivery; of the 14 pregnancies in the latter group, 12 living babies were born, 9 being delivered vaginally and 3 by cesarean section. These figures clearly indicate that the presence of pelvic ectopic kidneys in itself does not necessarily contraindicate pregnancy or mean that a pregnancy already in progress must be interrupted. However, although the majority of such women may be allowed to deliver vaginally, cesarean section is mandatory if all the renal tissue lies within the bony pelvis. Removal of a unilateral ectopic kidney is not indicated at the time of cesarean section unless the kidney is badly diseased and the opposite kidney is known to be normal.

Women with One Kidney.—Women with only one kidney, due either to previous nephrectomy or to congenital agenesis of the opposite kidney, can usually tolerate pregnancy without difficulty if the single kidney is normal. This is particularly true if the solitary kidney is on the left, since it normally undergoes less change during pregnancy than does the right, for reasons previously discussed. In persons with a congenital solitary kidney, the total renal function and renal mass are approximately the equivalent of two normal kidneys, and, in acquired cases, compensatory hypertrophy is complete within 18 months after nephrectomy, so that renal function and renal reserve are again normal. Therefore, subsequent pregnancies should be delayed at least 18 months after removal of one kidney, both to permit complete compensatory hypertrophy of the remaining kidney and to assure complete recovery from the original disease for which the opposite kidney was removed. There is no limit to the number of pregnancies that may occur in women with a single kidney without subsequent impairment of the kidney. As many as five have been reported in one woman.

Congenital Polycystic Renal Disease.—Congenital polycystic renal disease may be encountered during pregnancy. Exacerbation of the pathological alterations already produced by this entity may be expected in many instances, although many women with early polycystic disease without hypertension or infection tolerate pregnancy well and may not even be aware of having the disease. However, in those already harboring pyelonephritis or infection within the renal cysts, the infection may be expected to increase as the result of the superimposed changes induced by the pregnancy itself. The same is true of hypertension, which is present in 75% of people with polycystic renal disease, even without the added influence of pregnancy. It is advisable, therefore, to advise women with moderately advanced polycystic renal disease against pregnancy and to interrupt an existing pregnancy in those in whom hypertension, infection, and impairment of renal function become more severe during pregnancy.

Renal Tuberculosis

Renal tuberculosis is adversely affected by pregnancy because of the impairment of drainage of the kidneys, with consequent back-pressure, as well as the increased incidence of superimposed pyogenic pyelonephritis. It is generally agreed that pregnancy should not be permitted in women with moderate or advanced renal tuberculosis, whether unilateral or bilateral, and that it should be interrupted if the disease is discovered after gestation begins, unless the pregnancy is sufficiently advanced to permit premature delivery of a viable fetus. However, because of the modern advances in the chemotherapy of renal tuberculosis, pregnant women with early renal tuberculosis without pyelographic deformity may be adequately treated and the disease controlled during pregnancy by specific chemotherapy. Therefore, pregnancy may be permitted in such cases or allowed to continue if already in progress, especially if the parents are anxious to have an heir and are prepared to take the risks involved. There is no appreciable risk of infection of the fetus in such cases.

Renal Cancer

Fortunately, renal cancer is rarely encountered during pregnancy, since the lowest incidence of neoplastic renal disease occurs in the group of women of childbearing age (15 to 40 years of age).[10] However, if renal carcinoma is discovered during pregnancy, the kidney obviously should be removed if the opposite kidney is competent and no metastases are demonstrable. Continuance of the pregnancy afterwards, in such cases, is an individual problem, depending on its importance to the family and the prognosis of the mother's disease.

Renal Calculi

Because of the stasis of urine in the kidneys of pregnant women and the increased incidence of infection, the number of renal calculi discovered during pregnancy would be expected to be greater than in nonpregnant women. Arnell and Getzoff[11] reported calculi in 1 of 852 pregnant women, which they considered to be twice the incidence in nonpregnant women of comparable age. In reviewing 20 cases they noted no maternal deaths but a fetal mortality rate of 15%, due to spontaneous abortion. Twelve of the 20 women were erroneously thought to have pyelonephritis and were at first treated for this condition. Folger,[1] who reviewed 352 cases of women with stones seen on the urologic service at Western Reserve, noted that 86 became symptomatic for the first time during pregnancy. The incidence of the onset of symptoms was the same in each of the three trimesters as well as in the puerperium. Pregnancy had to be interrupted in only five cases.

Silent stones, impacted in a peripheral portion of the collecting system of the kidney and not producing obstruction, are well tolerated during pregnancy and require only chemotherapy to control infection if present. Stones producing obstruction at the ureteropelvic junction or becoming impacted in the ureter present an emergency. The first consideration is relief of the obstruction by passage of a ureteral catheter into the kidney if possible. If a catheter can be passed, it should be left indwelling. After the symptoms have been controlled and renal function has been restored, definitive treatment can then be planned, depending on the size and position of the stone and the stage of the pregnancy. A stone within the ureter small enough to pass spontaneously may be given an opportunity to do so after an appropriate interval of drainage of the kidney and dilatation of the ureter by indwelling catheters. Those too large to pass either must be removed surgically during the pregnancy or, if the pregnancy is near term, continuous ureteral catheter drainage of the kidney should be employed until after delivery, when the stone can be removed either by open operation or by cystoscopic manipulation. In women whose stones are causing complete obstruction and in whom it is impossible to pass a ureteral catheter to the kidney, immediate surgical removal of the stone is mandatory, regardless of its size or position.

Operative Procedures During Pregnancy

If an elective operation on the upper urinary tract is being considered during pregnancy, several factors concerning the pregnancy itself become important in influencing the choice of time for operation. Transfer of the site of formation of estrogen and progesterone from the ovary to the placenta is probably gradual, being complete between the second and third months of gestation. By the fourth month the growing ovum entirely fills the uterine cavity, placental formation is complete, and the fetus is securely anchored to the uterine wall. The optimum time, therefore, for elective surgical procedures is after the 18th week. Before the 18th week the postoperative incidence of spontaneous abortion is high, for the reasons already mentioned. After the seventh month of gestation, delivery of a viable fetus can be expected, a fact that may sometimes influence the decision as to the choice of time for elective operation.

Preoperative preparation should include administration of the usual sedatives the night before, and also the morning of, operation. Patients with a history of threatened abortion require more careful preparation. In such cases a daily injection of 100 ml. of progesterone in oil should be administered to attempt to preserve the pregnancy. Administration of the hormone should be started one or two days before the contemplated operation if possible and continued as long as necessary postoperatively. However, in women who have had no difficulty up to the time of operation, hormone therapy is unnecessary. Several new drugs are now being investigated for use in threatened premature labor. A spinal anesthetic is preferable in most cases. Early ambulation is encouraged postoperatively, except in cases of threatened abortion.

Comment

Any woman with a known history of renal disease or hypertension who contemplates pregnancy should have a complete urologic examination before pregnancy is permitted. This should include careful examination of the urine for infection by smear and culture, renal function tests, and excretory urograms supplemented by retrograde pyelography when indicated. Since hypertension is one of the more common complications of pregnancy and although it is often associated with eclampsia or else is of the essential type, the possibility of an abnormality of the urinary tract should never be overlooked. Among the more important possibilities in addition to nephritis are unilateral atrophic pyelonephritis, polycystic renal disease, or bilateral obstructive hydronephrosis with pronounced impairment of renal function. The indications for therapeutic abortion in the presence of surgical renal disease must necessarily be individualized and the decision regarding interruption of the pregnancy considered in the light of the nature and extent of the renal disease, the general health of the patient, and, in borderline cases, the attitude of the patient and her husband regarding the importance of the anticipated child to them.

Summary

The urinary tract is one of the commonest sites of complications of pregnancy. The physiological changes occurring during pregnancy consist in dilatation of the upper two-thirds of the upper urinary tract, with impairment of drainage and resultant stasis of urine and back-pressure in the renal pelves. These changes are due to both hormonal and mechanical factors incident to pregnancy. In anticipation of these changes, any known preexisting surgical renal disease should be carefully evaluated by complete urologic study before pregnancy is permitted. The indications for therapeutic abortion in the presence of surgical renal disease discovered during pregnancy vary with the individual case. The decision must be based upon the nature and extent of the renal disease, the general health of the patient, and the risks that the parents are prepared to take to obtain an heir. Upper urinary tract surgery may be performed during pregnancy when necessary, without undue risk to the patient or the fetus, after careful selection of the optimum time for surgery and the proper preparation of the patient.

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SURGICAL INJURIES OF THE URETER AND BLADDER

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• The ureters and bladder are liable to injury during surgical operations on other structures within or about the pelvis. How this can happen is shown in nine case histories, six of them involving hysterectomy, one a lumbar laminectomy, one a colpotomy with transection of the uterosacral ligaments, and one a cesarean section. The surgical treatment of the individual cases was successful, but more important are the means to be used in preventing such injuries. A catheter should be inserted during operations near a ureter, to aid in identifying and avoiding it. If it is ligated, severed, or otherwise injured, it should be repaired at the time. If there is danger of kinking, a soft ureteral catheter can be left in place four to six days postoperatively. Urinary symptoms developing after a pelvic operation require prompt and precise diagnosis. This is usually not difficult, once the possibility of this complication is borne in mind.

Accidental surgical injury to the ureter and bladder has always been frequent in association with pelvic surgery. Improved methods of anesthesia and replacement therapy have enabled the gynecologist to do more radical procedures, and, as a result, the incidence of ureteral and bladder injuries has increased. Also, improved diagnostic methods have brought about an increase in the total number of pelvic operations. The diagnosis of surgical injury to the ureter and the bladder is usually not difficult, once the possibility of this complication is borne in mind. Intravenous urograms followed by cystoscopy will make or exclude a diagnosis of ureteral injury. An opaque cystogram or injection of methylene blue into the bladder with the vagina packed is the usual method for determining the continuity of the bladder; cystoscopy may be used but usually is of less value. Injury to the ureters or bladder, when recognized at the time of surgery, should be repaired immediately.

No attempt will be made in this report to review the literature. The purpose of this report will be to briefly present a case illustrating each of the various types of ureteral and bladder injuries and a method of management, followed by suggested preventive measures in some types of injuries. The routine use of ureteral catheters, prior to a difficult hysterectomy, would eliminate most of the ureteral injuries.

Report of Cases

Case 1.—This 33-year-old woman with a left ureterovaginal fistula was seen three weeks after a hysterectomy. The ureteral injury was recognized at the time of surgery, and a ureteral catheter was left indwelling for two weeks; however, the site of the ureteral injury was not drained. After surgery, the patient had a constant vaginal drainage of urine and x-ray pictures demonstrated a fistula (fig. 1). A polyethylene tube (8 F.) was passed to the left kidney, meeting only mild resistance, and was left indwelling for 10 days. The vaginal drainage of urine ceased and the patient had an uneventful recovery, except for an episode of acute pyelonephritis caused by Aerobacter aerogenes. A urogram made eight months postoperatively showed a normal left urinary tract (fig. 2).

If a Penrose drain had been passed down to the site of the ureteral injury and brought out retroperitoneally through a stab wound, a ureterovaginal fistula probably would not have developed. Use of a ureteral catheter prior to hysterectomy would have prevented the injury.

Case 2.—This 45-year-old woman was seen because of a watery vaginal discharge for one month after an abdominal hysterectomy. Urologic examination revealed a ureterovaginal fistula, with obstruction to the intramural portion of the left ureter (fig. 3). At the time of operation, the left ureter was found to be ligated as it entered the bladder. The ureter above the site of ligation was dilated and tortuous. The ligated segment was sectioned and the proximal ureter spatulated, turned back in a cuff-like fashion, and reimplanted into the bladder through the original ureteral orifice. A pyelogram made one year later revealed normal renal function (fig. 4), and the cystogram showed no ureteral reflux.

Reimplantation of the ureter in the bladder as described above produces a ureteral stump in the bladder that prevents ureteral reflux. Again use of a ureteral catheter prior to hysterectomy would have prevented injury.

Case 3.—This 40-year-old woman was seen because of vaginal drainage of urine for three months after an abdominal hysterectomy for fibromyomas. Examination revealed a left ureterovaginal fistula and a severe cystitis due to A. aerogenes, with a bladder capacity of 3 oz. For two weeks many drugs were used without results, so drug sensitivity studies in vitro were done and revealed nitrofurantoin (Furadantin) to be the drug of choice. After one week's therapy with this drug, the bladder capacity returned to normal and the culture became negative. An exploratory operation on the lower part of the left ureter was then performed (by Dr. Dexter Amend); this revealed that the ureter ended in a fibrous mass proximal to the bladder (fig. 5). A segment of ureter 8 cm. long was missing, and a bladder flap after the technique of Ocherbold was used to bridge the defect. A polyethylene tube was left indwelling as a splint for 10 days postoperatively. A ureterogram and a cystogram made postoperatively (fig. 6 and 7) revealed no narrowing at the site of anastomosis or reflux of urine, respectively, four months later.

It has been stated that reflux follows this method of repair; such has not been our experience, as shown in the cystogram. Complete eradication of the severe long-standing cystitis due to A. aerogenes by the use of nitrofurantoin made the operation possible.

Case 4.—This 30-year-old male was seen four weeks after a lumbar laminectomy.[1] Immediately after the laminectomy, a mass developed in the left lower quadrant, which was incised and drained urine continuously. Urologic examination revealed a urinary fistula in the left lower quadrant and a grade 3 hydronephrosis on the left, with an occlusion of the left ureter at the junction of the upper two-thirds with the lower one-third (fig. 8). Exploration of the left ureter was carried out one month after

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Read before the Joint Meeting of the Section on Obstetrics and Gynecology and the Section on Urology at the 105th Annual Meeting of the American Medical Association, Chicago, June 14, 1956.

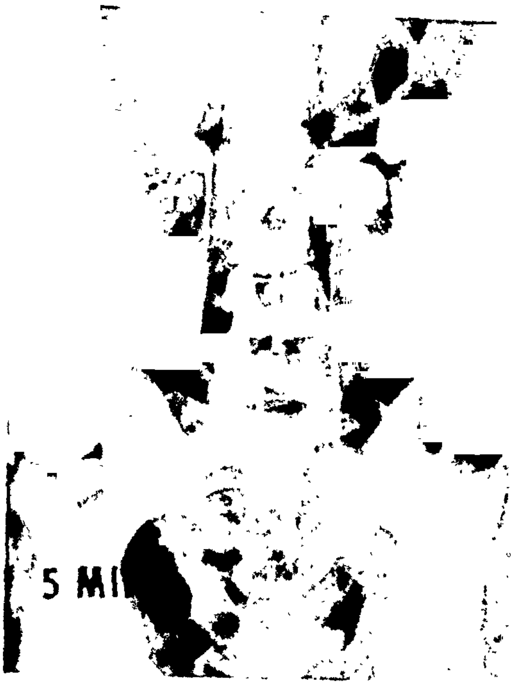

Fig. 1 (case 1).—Intravenous urogram with extravasation of dye from left lower ureter.

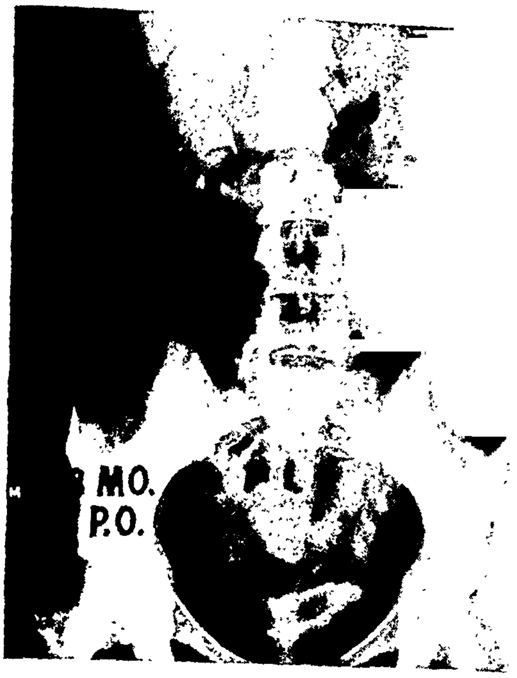

Fig. 2 (case 1).—Intravenous urogram made eight months postoperatively.

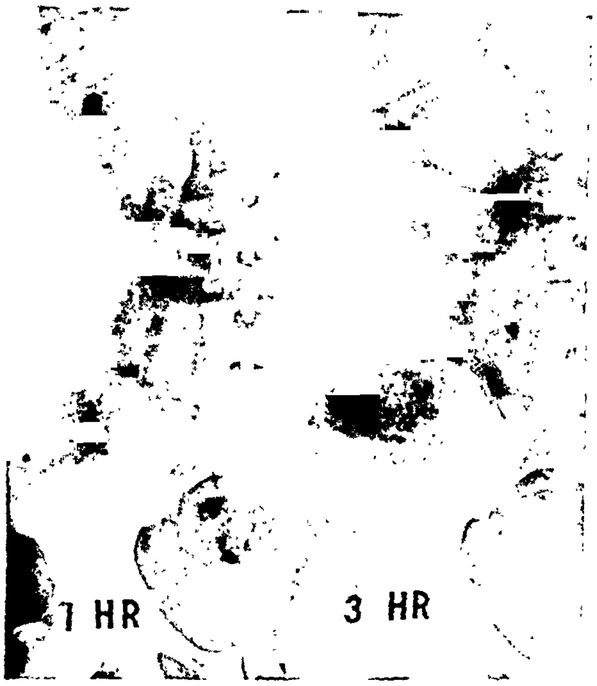

Fig. 3 (case 2).—Intravenous urogram (one hour) and attempted retrograde pyelogram, showing occlusion of terminal ureter.

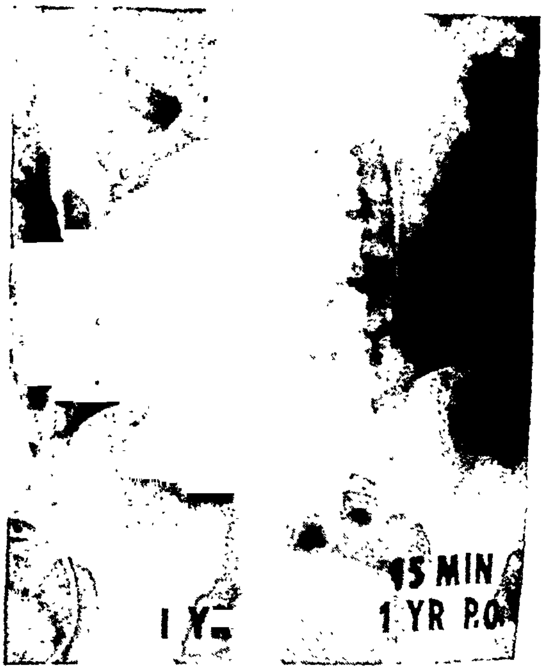

Fig. 4 (case 2).—Intravenous and retrograde urogram made one year after reimplantation of left ureter into bladder.

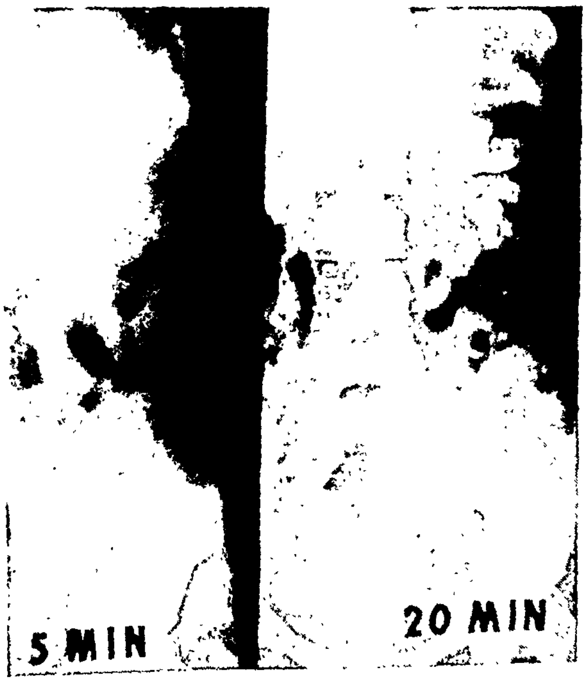

Fig. 5 (case 3).—Intravenous urogram made preoperatively, revealing hydronephrosis and displacement of bladder.

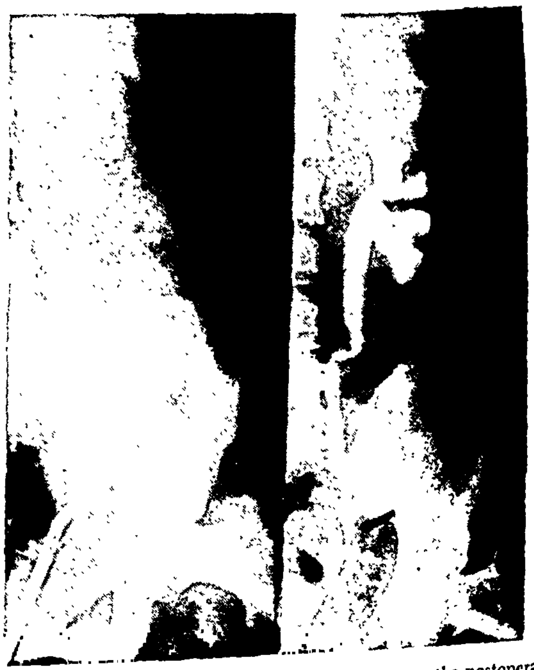

Fig. 6 (case 3).—Retrograde urogram made four months postoperatively.

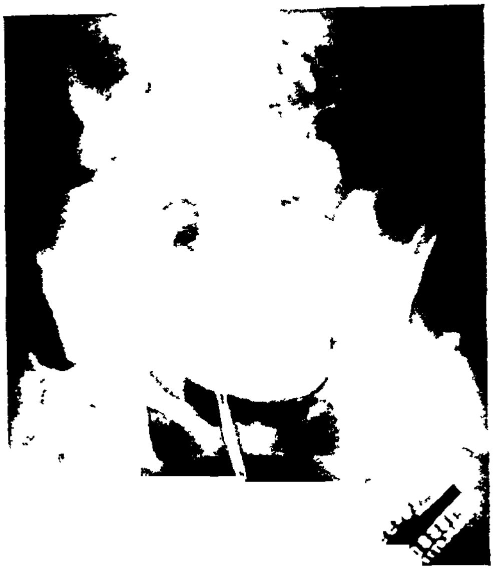

Fig 7 (case 3) —Cystogram made four months postoperatively without ureteral reflux

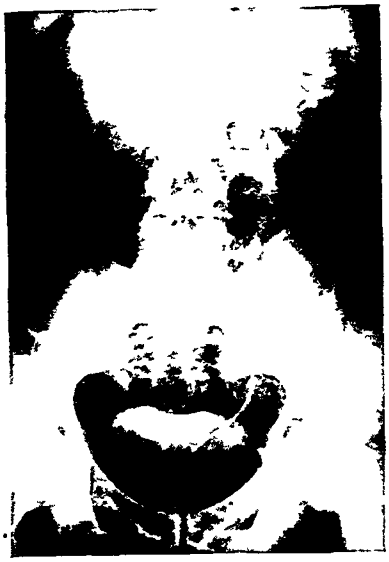

Fig 9 (case 4) —Retrograde pyelogram made eight months postoperatively

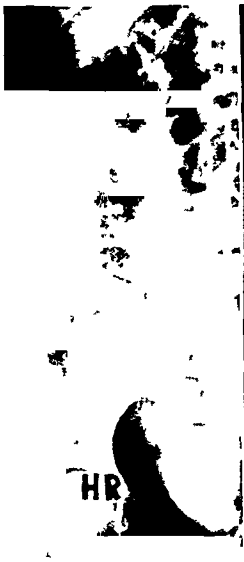

Fig 10 (case 5) —Intravenous urogram made preoperatively, revealing very little dye one hour after injection

Fig 11 (case 5) —Intravenous urogram made one year later

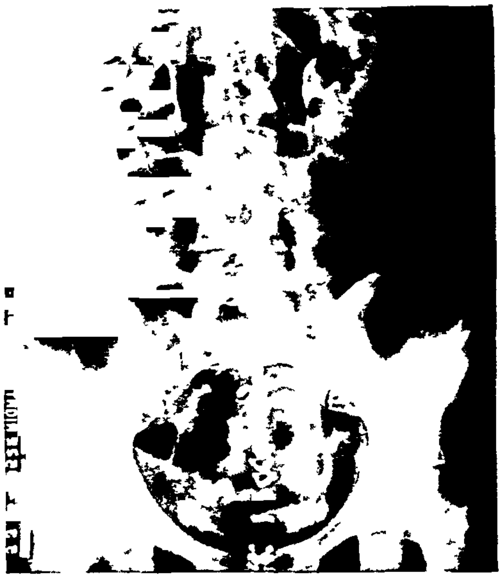

Fig 12 (case 6) —Intravenous urogram showing poor function and marked hydronephrosis on the right

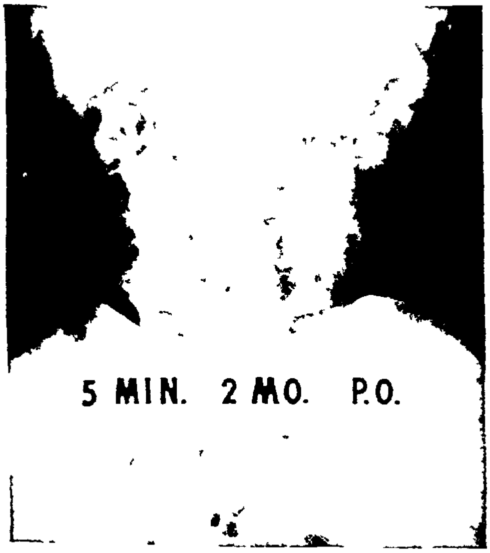

Fig 13 (case 6) —Intravenous urogram made two months postoperatively, with normal function and collecting system on the right

Fig. 14 (case 8) —A urethral catheter passing through vesicocervical fistula into vagina Dye has been injected through catheter into vagina

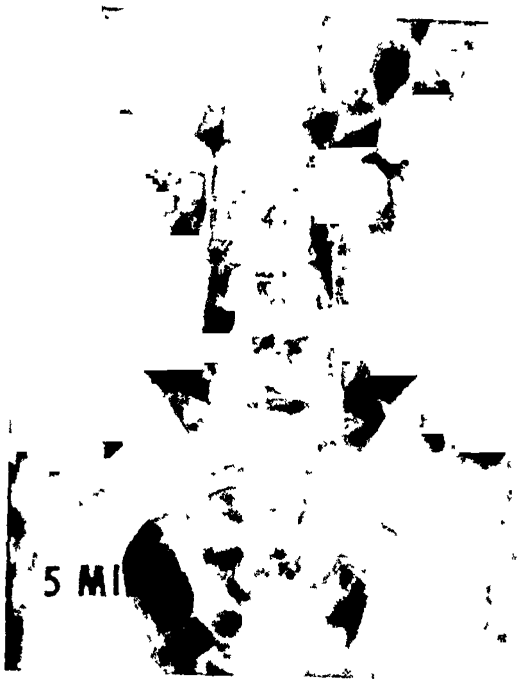

Fig. 1 (case 1).—Intravenous urogram with extravasation of dye from left lower ureter.

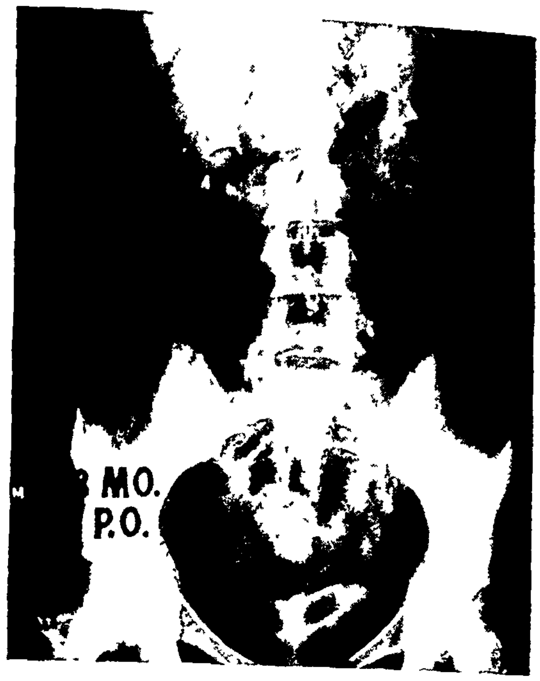

Fig. 2 (case 1).—Intravenous urogram made eight months postoperatively.

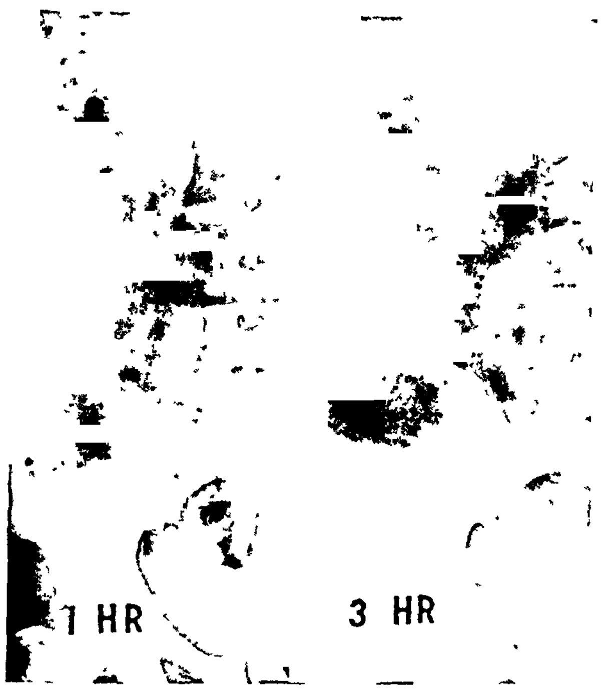

Fig. 3 (case 2).—Intravenous urogram (one hour) and attempted retrograde pyelogram, showing occlusion of terminal ureter.

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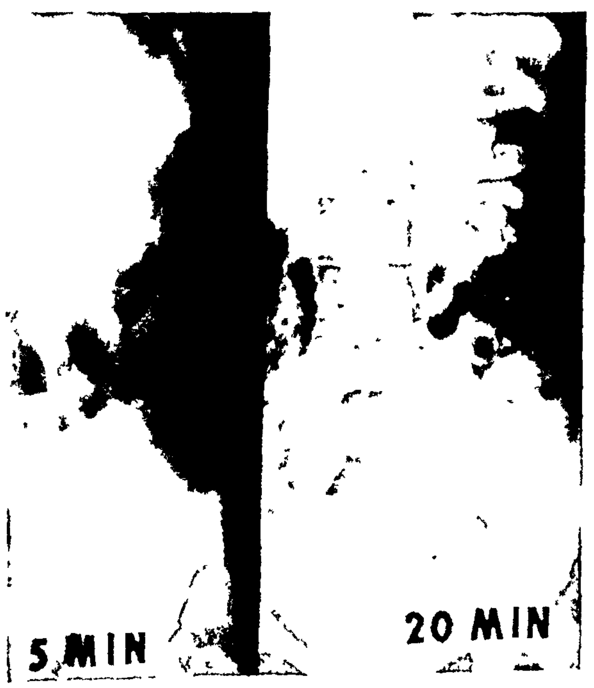

Fig. 5 (case 3).—Intravenous urogram made preoperatively, revealing hydronephrosis and displacement of bladder.

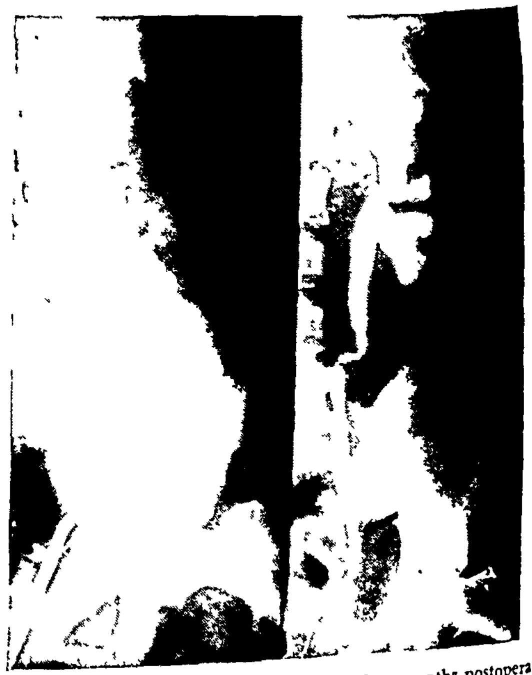

Fig. 6 (case 3).—Retrograde urogram made four months postoperatively.

Summary

Most ureteral injuries can be avoided by the use of soft ureteral catheters during difficult pelvic surgery. If a ureteral injury is discovered during surgery, it should be repaired immediately. A ligature around the ureter found after surgery should be removed as soon as the patient's general condition permits. A completely severed ureter should be repaired by using interrupted vertical mattress sutures so as to evert the two cut ends. Ureteral reflux has not occurred after reimplantation of the ureter into the bladder when a cuff of the ureter projects into the bladder.

Bladder injuries when discovered during operation should be repaired then, but, if discovered later, the repair should be delayed for four to eight weeks.

1012 Kings Dr. (Dr. Baird).

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PATHOLOGICAL LESIONS OF THE FEMALE URETHRA

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and
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• *Abnormalities and diseases of the female urethra include the caruncle, diverticula, cysts, carcinoma, urethritis, trigonitis, venereal infections, and the unusual conditions of polyps and congenital valves. Over a 20-year period of observations, it was found that prolapse of the posterior margin of the mucosa at the urethral meatus was extremely common after the menopause, although it may also occur in younger women and children. Of 108 pathological specimens of the female urethra, 71 were urethral caruncles. The common caruncle rarely is malignant and, unless symptomatic, often requires no treatment. Other treatment for pathological conditions of the female urethra depends not only on the lesions observed but, occasionally, on related syndromes such as anxieties and allergies.*

The short tubular structure representing the female urethra is subject to a surprising variety of abnormalities, because of its position, delicate membranes, attached ducts and glands, developmental variations, occasional venereal diseases, changes in natural hormones, and even the stress and strain of life. Study of specimens from the female urethra, obtained over a period of 20 years in the Louisville General Hospital and in private practice, has led us to summarize and describe the following lesions.

Venereal Diseases

The urethral meatus of the female may be affected by the venereal diseases, including the temporary chancre of syphilis, acute or chronic gonorrheal infection in Skene's ducts, probably the chancroid and granuloma inguinale, and particularly the ulcerative destructive lesions of venereal lymphogranuloma. Formerly, it was thought that all infections of Skene's ducts were gonorrheal in origin. While the gonococcus thrives in that environment and must be considered as an etiological agent, Trichomonas vaginalis is considered to be the more common offender today. The Trichomonas infection produces minute red dots around the meatus (and vestibule also) and may produce a caruncle of reddened, edematous appearance and the chronic white discharge that may be milked from the urethra over a period of years. Shelanski and Savitz[1] in 1939 pointed out the relationship of T. vaginalis infestation to Bartholin's gland (with secondary invaders) and infections of Skene's ducts; more recently, in 1955, Kean[2] has emphasized the frequent finding of T. vaginalis in the urethra of women. Infection from this obstinate organism rarely requires direct manipulation of the urethra, caruncle, or Skene's ducts but does necessitate persistent and prolonged antitrichomonacidal treatment to the vagina. Apparently T. vaginalis infections may or may not be acquired by sexual intercourse; they are commonly nonvenereal.

The urethral syndrome of venereal lymphogranuloma, described by Gray[3] in 1936, apparently begins as a chronic urethritis, with or without intraurethral ulceration, which may remain extremely chronic and indolent or may proceed to urethral stricture or to ulcerative destruction of the urethra; the ulceration may extend beneath the clitoris and labia or about the introitus and deeply to the sides of the rectum; and elephantiasis vulvae may be associated. This disease, diagnosed by exclusion and by the intradermal Frei test, producing severe chronic inflammation with no specific microscopic characteristics, is seen where venereal disease is common, is extraordinarily rare in a usual practice, and is apparently decreasing in incidence. The United States Public Health Service indicates that 2,603 cases of venereal lymphogranuloma were reported in the United States in 1946, but only 875 cases in 1955. The incidence of all venereal diseases has declined over these years.

Verruca acuminata (condyloma acuminatum), or common wart about the genitalia, is attracted by the urethral meatus. In 108 specimens of lesions of the urethra, reported in this paper, 8 showed the benign squamous cell proliferation on papillary folds characteristic of this virus disease. The extreme proliferation of squamous epithelium and numerous mitoses at times require consideration to assure the benign

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Read before the Joint Meeting of the Section on Obstetrics and Gynecology and the Section on Urology at the 105th Annual Meeting of the American Medical Association, Chicago, June 14, 1956.

character of the lesion. This so-called venereal wart may be transmitted by sexual intercourse, but it may be acquired without such a social contact. These were treated by excision, administration of podophyllin, and probably best by fulguration.

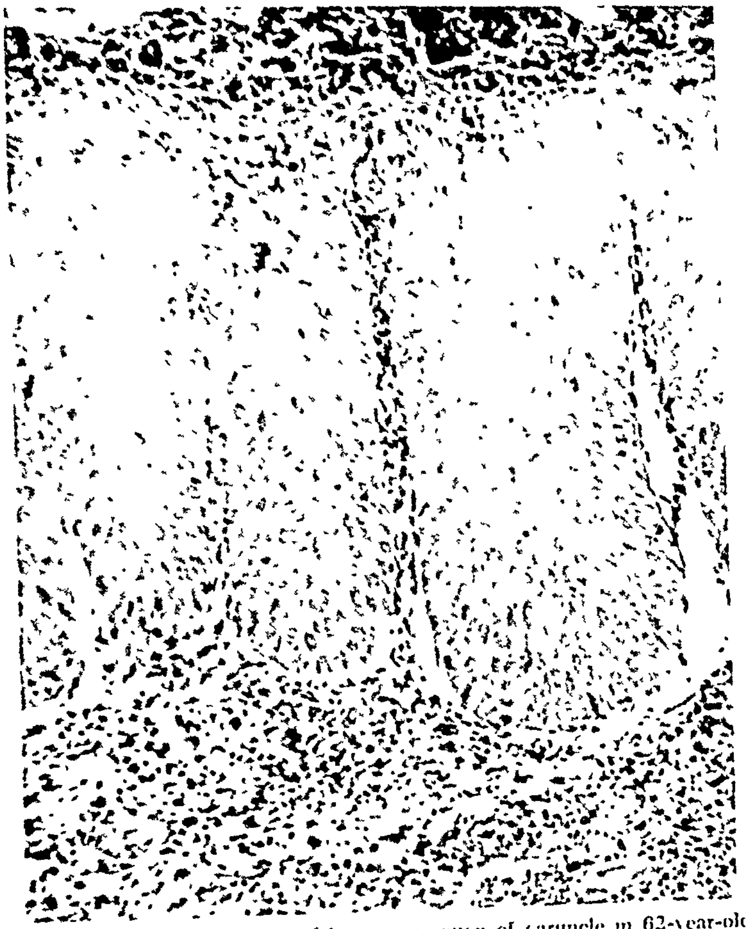

Fig. 1.—Photomicrograph of biopsy specimen of caruncle in 62-year-old woman before treatment with estrogen cream.

Urethral Caruncle

Prolapse of the posterior margin of the mucosa at the urethral meatus is extremely common after the menopause, but may occur in younger women, including children. Small caruncles commonly cause no symptoms; large ones may produce few complaints. It is not a tumor. Slight burning discomfort, soreness, pain on urination, and dyspareunia require treatment. Occasionally the pain is severe. Infections of the urethral meatus and Skene's ducts may be causal factors. Absence of estrogenic hormone, after the menopause, causes atrophy of the urethral and vaginal epithelium, with susceptibility to irritation, inflammation, and infection. Perhaps the lack of hormone also loosens the lining mucosa.

After studying 91 specimens of benign lesions from the urethral meatus, we have considered that 71 are true caruncles, 12 are granulomas, and 8 are verruca acuminata (mentioned above). The true caruncles have been divided into three groups by us, according to their surface epithelium, which suggests the point of origin. Others have separated the angiomatous type, but the dilated and proliferated vessels are likely related to the prolapse, edema, and inflammation. The granulomatous type of caruncle seems separate, being a primary infection, in contrast to accented prolapse of the mucosa in the true caruncle.

Group 1.—Sixteen of the caruncles had a surface completely covered with stratified squamous epithelium. Of these, 10 contained no glands and 6 contained gland spaces lined by transitional epithelium. Thirteen of these specimens were from postmenopausal women. Inflammation associated with proliferation of small vessels varied from slight to severe.

Group 2.—In 28 specimens the surface of the caruncle was covered by stratified squamous and by transitional epithelium. In 20 of these, there were no glands; 8 contained glands lined by transitional epithelium; and 9 were from postmenopausal women. Four patients were quite young (aged 9, 11, 14, and 19).

Group 3.—In 27 specimens, the caruncle was covered entirely by transitional epithelium and all contained transitional glands. The degree of inflammation varied. In two patients, aged 38 and 17, the caruncles showed marked mucous secretion of the glands; the specimen from the former case originally was considered to represent a low-grade adenocarcinoma, was excised locally, recurred as a slight caruncle five years later, and showed a clearer transitional epithelial gland pattern at the last biopsy. Of this third group of 27, one was from a patient 3 years old and one from a 10-year-old patient, but 20 were from postmenopausal patients.

Of the entire 71 caruncles, 9 showed cellular atypia, involving the transitional glands in five cases and the prolonged rete pegs of the squamous epithelium in four, the latter attributed to inflammation. The transitional cell changes are to be carefully distinguished from carcinoma, as an error may be made in each direction. As a rule the carcinomatous change must be very clear. At least 13 patients with caruncles had no complaints before excision or fulguration, but some developed complaints subsequently.

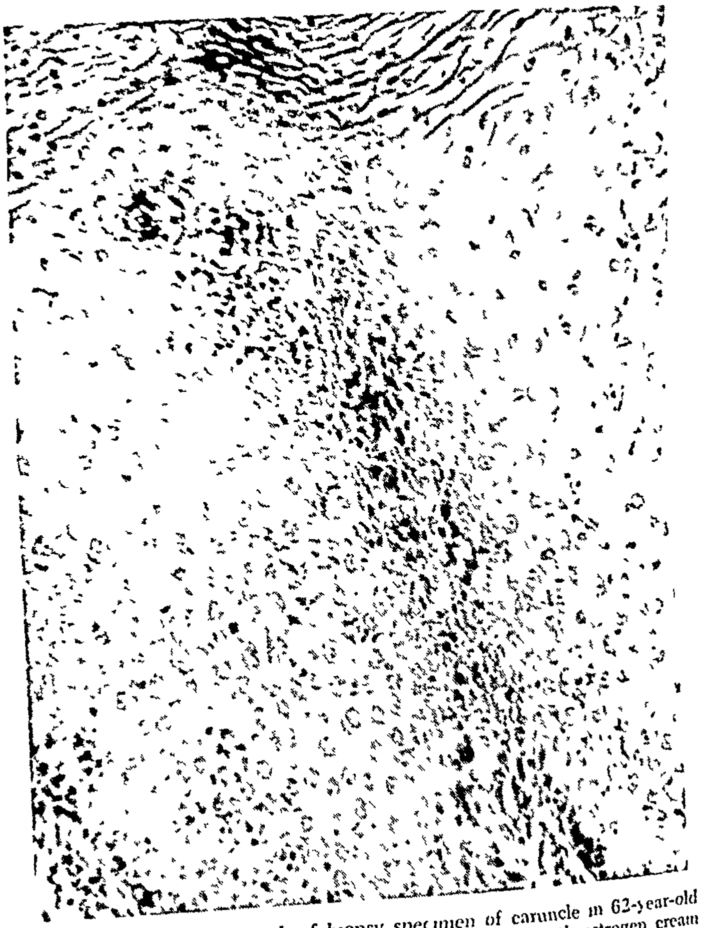

Fig. 2.—Photomicrograph of biopsy specimen of caruncle in 62-year-old woman (see fig. 1) after 21 days of local treatment with estrogen cream (Estrone sulfate).

In 12 other cases the diagnosis was considered granuloma, because of severe, nonspecific, inflammatory reaction. Three showed no surface epithelium, and nine specimens were partially covered with stratified squamous epithelium. The origin here seemed a definite infection, possibly venereal (average age of patients, 39 years). Perhaps several of the previous cases considered caruncles should be included with the granulomas, as some had marked inflammation.

Biopsy has been performed in only a small percentage of caruncles in our care of patients. The majority had no treatment. In the case of a large or angry lesion, one showing any brittleness, hardness, or surrounding induration, one bleeding easily, or one requiring general anesthesia and fulguration, biopsy was always performed before treatment. Often satisfactory improvement followed treatment of T. vaginalis infection, or the use of oral or local estrogenic therapy in older women (fig. 1 and 2). Because of the great frequency of the urethral caruncle, small or large, and the rarity of carcinoma of the urethra, we believe that the ordinary caruncle represents very slight risk to the patient and that treatment is primarily indicated to relieve symptoms.

Prolapse of the urethra, a circular prolapse in contrast to the more common posterior prolapse of the caruncle, was observed in two cases. One was in a child 3 years of age, and one was in a postmenopausal patient. They were treated by ligation around a catheter and circular excision, with resuture around the meatus.

Urethral Diverticulum

Urethral diverticula may be of acquired or congenital origin (Nel[4]). The acquired sac develops after perforation or local dilatation, usually after infection, abscess, and rupture of a paraurethral gland. The trauma of parturition is a factor in some cases. The congenital types arise from Gartner's ducts, faulty union of primal folds, cell rests, Müllerian remnant cysts, or congenital dilatation of paraurethral ducts. The diverticulum may or may not have the muscular layers of the urethra about it and may be lined with squamous, columnar, cuboidal, transitional epithelium or by granulation tissue only.

In some there are no symptoms. In others there may be pain in the lower abdomen, suprapubic, or perineal areas; pressure, weight, or pain in the vagina; pain radiating up into the pelvis when sitting; burning discomfort, severe dysuria, severe frequency; recurrent cystitis; or dribbling after voiding. Pain at the end of urination and dyspareunia are frequent complaints. The diverticulum may remain undiscovered even after long investigation and treatment. The soft sac often is not palpated, but milking the urethra during vaginal examination may produce purulent fluid and prompt the diagnosis. Demonstration of the orifice at cystoscopy, whether by the direct vision endoscope or the panendoscope, may be difficult. Filling the sac for radiographic visualization may be unsatisfactory.

Complications include infection with abscess, which may require incision and drainage. Calculi form occasionally. Three cases of malignancy—an epithelioma, a mucous-secreting adenocarcinoma, and a transitional cell carcinoma—have been reported in three studies (Walters and Thiessen,[5] Hamilton and Leach,[6] and Wishard and Nourse[7]).

Diverticula should be excised because of proximity of the infected sac to the bladder and for relief of symptoms. Various methods have been suggested, including incising the meatus down the urethra into the sac, with subsequent excision and repair (Edwards and Beebe[8]). Meticulous excision of the sac itself, with closure in layers, using 0000 absorbable surgical sutures in the mucosa, retention catheter for 10 days, and antibiotic therapy gave good results in our hands (fig. 3).

Thirteen cases of urethral diverticula were studied in this series. Four specimens were lined by stratified squamous epithelium, two by transitional epithelium, two by a single layer of columnar epithelium, and five by granulation tissue. Two of the latter showed small tubular glands with columnar cells extending into the wall of the diverticulum. One resembled carcinoma, but the apparent invasion was attributed to the inflammation and the patient was well after five years.

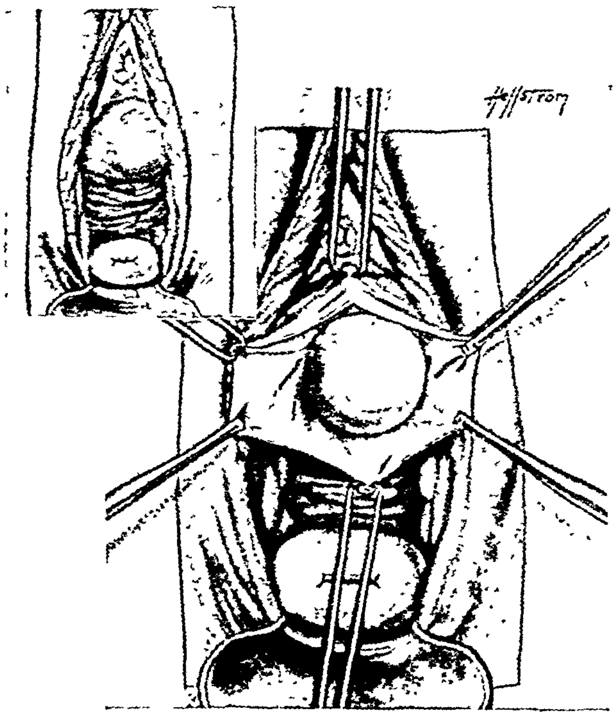

Fig. 3 —Excision of suburethral diverticulum

Postoperative complications may include fistula, stricture, or recurrence. In this series of 13 cases, one patient developed a fistula that healed after four months, one had severe postoperative bleeding from the operative site, and one developed a recurrent diverticulum. This was cured after reexcision.

Suburethral Cysts

Suburethral cysts are less common than diverticula. They may arise from a diverticulum with sealed neck, but more often arise from Müllerian duct remnants or detached urethral glands. Occasionally they cause severe pain, perhaps due to trauma and rapid enlargement, but usually they are asymptomatic. These cysts may extend up around the urethra on one side or the other. A similar lesion is the subvesical cyst, which may extend far up alongside the cervix and be removed with difficulty. Two patients with excised cysts had a lining epithelium of flattened transitional epithelium, one with transitional glands in the wall. There was no inflammation. Excision should be performed carefully but should be complete.

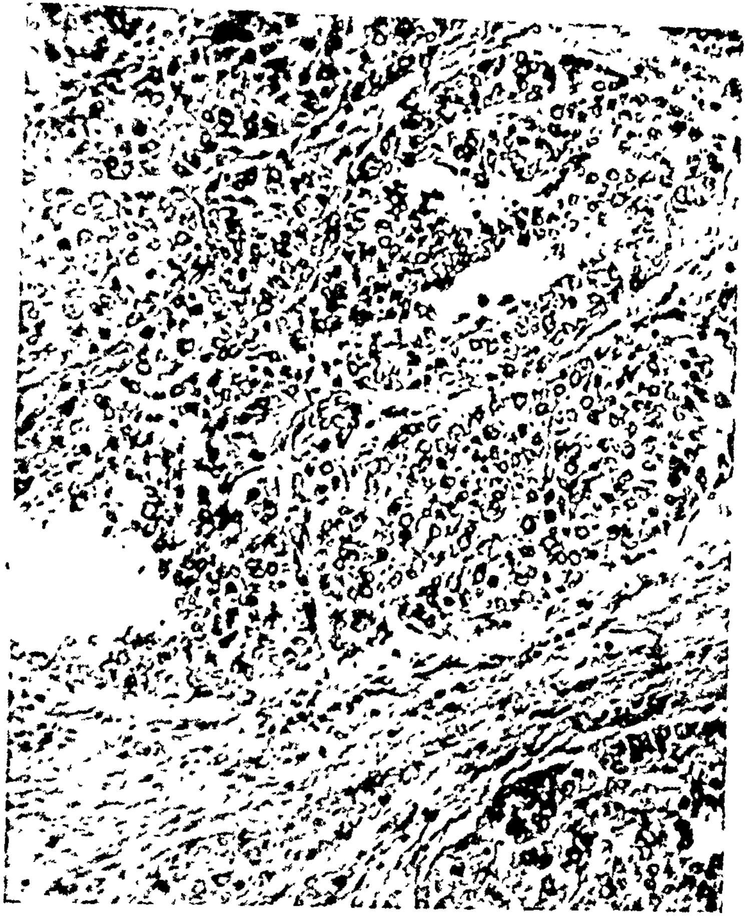

Fig. 4 (case 1).—Photomicrograph of transitional cell carcinoma, rapidly growing.

Carcinoma of the Urethra

Some 600 cases of carcinoma of the female urethra have been reported to date. Symptoms include hematuria, severe dysuria, and swelling. Approximately half the patients have given a history of chronic irritation or of caruncle treated previously. The gross appearance is that of a firm, rolled-out granular growth, an indurated ulcer, or, more rarely, the entire urethra may be encircled with infiltrating tumor. Ritter[9] described four types: exophytic squamous cell type, endophytic squamous cell type, adenocarcinoma (much less common), and rare miscellaneous tumors, including sarcoma and melanoma. Origin from transitional epithelium with variable degree of proliferation probably is more frequent than origin from squamous epithelium near the tip of the urethra. Metastases to inguinal nodes have been common and apparently occur early. Most clinicians advise operative removal with or without postoperative irradiation, but results have been discouraging. Radical excision has been tried recently. Brack and Farber[10] reported 10 cases and recommended relatively heavy radium and x-ray therapy, with consideration of later excision. Removal of the inguinal nodes is advisable. Most authors agree that the treatment of choice is surgical excision, but it may be that rapidly growing, anaplastic tumors should have irradiation therapy. We have had only two cases of cancer in this series. One was in the Louisville General Hospital, and one in private practice.

Case 1.—A patient, aged 49, developed frequency, urgency, nocturia, intense constant pain in the urethra, and difficulty in starting urination in September, 1951. On Oct. 31, 1951, a severe urethral stricture was found. On Dec. 5, 1951, the meatus was everted, with rolled-out, firm edges; the entire urethra was indurated and pipe-like; and the vesical neck was irregular with ragged tissue on the inner margin. Biopsy showed infiltrating carcinoma (fig. 4). Ureteral transplantation to the sigmoid was performed. On Jan. 8, 1952, the urethral tumor was fixed to the symphysis, and there was extension beneath the bladder on the left. On Jan. 17, 1952, the bladder, uterus, vagina, and symphysis pubis were removed (by Dr. R. A. Griswold). A right lateral mass in the obturator foramen could not be excised; biopsy showed metastatic carcinoma. The patient died March 12, 1952, after a complicated course and while receiving x-ray therapy. This patient had a very rapidly growing, infiltrating transitional cell carcinoma made up of relatively small cells, with numerous mitoses. The tumor developed from a urethral stricture in two months to involve the entire urethra and to invade local structures and the symphysis pubis. Apparently within this short duration it had become inoperable.

Case 2.—This 75-year-old woman complained of a severe bearing-down pain, bleeding, incontinence of urine, and marked sensitivity of vagina and vulva for three months. Examination showed ulcerative destruction of the anterior urethra, with extremely tender nodular tumor, interpreted on biopsy as a papillary transitional cell carcinoma, grade 2 (fig. 5). The tumor, clitoris, and bladder neck were resected on June 5, 1953, closing the bladder neck around a Foley catheter. (A conservative operation was elected because of the age of the patient.) Pain was relieved, but the area was not satisfactorily dry. On Jan. 8, 1954, after slow local recurrence and increasing pain, anterior exenteration was performed, removing the bladder, uterus, and vagina, and transplanting the ureters to the sigmoid. The postoperative course was not difficult, but 24 days later the patient died of a

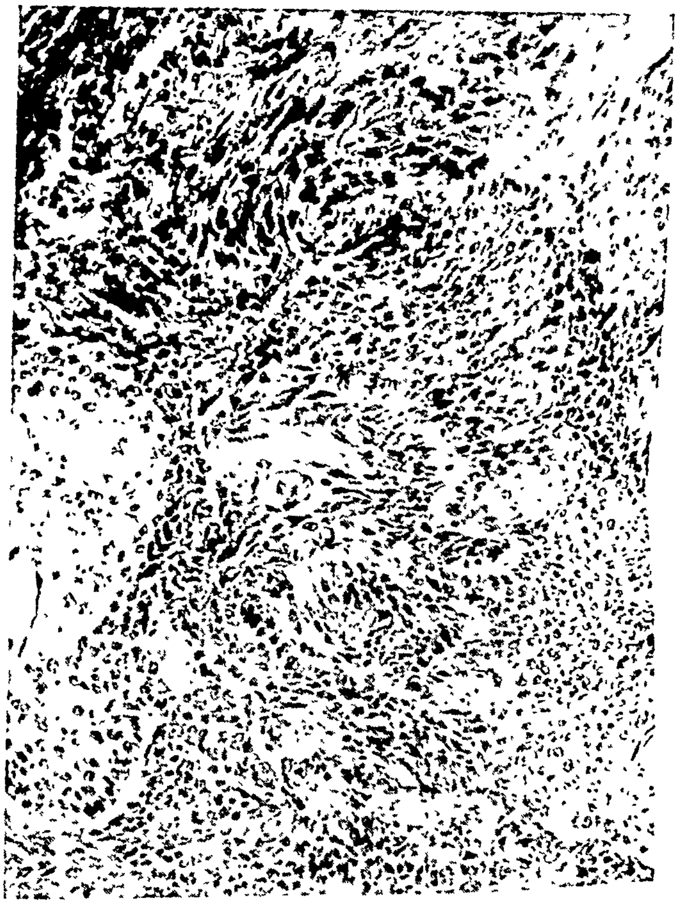

Fig. 5 (case 2).—Photomicrograph of transitional cell carcinoma, relatively slowly growing.

cerebral attack at home. Postmortem examination, limited to the abdomen, showed no infection, no residual tumor, and satisfactory healing of the ureteral transplants, without stricture.

It seems that a slowly growing tumor with a long history may be better treated by wide excision alone but that a rapidly growing tumor may be better treated by intensive irradiation and subsequent excision if deemed advisable. While malignancy of the urethra is not common, early diagnosis is important.

Unusual Lesions of the Urethra

Everett and Brack[11] recently described unusual lesions of the female urethra, discovered only by painstaking study with the panendoscope. These included congenital valves in children, minute urethral diverticula, and urethral polyps. The symptoms were recurring cystitis, intermittent hematuria, dysuria, and eneuresis. Schloss[12] described caruncles of the posterior urethra and bladder neck that produced symptoms of "irritable bladder" and "chronic urethritis." These were treated by resection.

Chronic Urethritis and Trigonitis in Women ✓

Urinary frequency, burning, and pain, in the absence of pyuria and with negative cultures, long have been attributed to chronic urethritis and trigonitis. Various treatments have included the application of dilute solutions of silver nitrate, fulguration of the bladder neck and urethra, resection of the bladder neck, dilatation of the ureters, and, most popular of all, repeated dilatation of the urethra. Numerous antiseptics have been used locally. Allergic phenomena have been implicated as a common cause by some authors (Powell and Powell[13]).

The syndrome occurs mainly in those with great nervous tension and severe anxieties. It is remarkable how often a single severe emotional jolt seems to have precipitated these difficulties. Resolving a personal problem (unfortunately frequently impossible), reassurance, and use of tranquilizing drugs seem of more value than local urologic treatments. Our success has been limited after dilatations and local therapy.

Summary and Conclusions

Venereal diseases of the urethra in females include gonorrhea and venereal lymphogranuloma. The incidence of both has greatly decreased. Chronic infection in Skene's ducts more commonly is due to Trichomonas vaginalis. The latter may or may not be transmitted by sexual contact. Verrucae acuminatae (condylomata acuminata) are not uncommon (occurring in eight cases in this study).

Study of 108 pathological specimens of lesions of the female urethra revealed the following findings: 71 urethral caruncles had a surface of squamous epithelium in 16, of combined squamous and transitional epithelium in 28, and of transitional epithelium alone in 27. Forty-two patients had passed the menopause. Lack of estrogenic hormone seems a factor in many of these cases, and the lesion tends to regress after application of estrogenic creams. In younger women, infection, including T. vaginalis infection, is a factor and may necessitate prolonged treatment of the vaginitis. The common caruncle rarely is malignant. Usually it is asymptomatic, and often no treatment is indicated.

Twelve specimens showed granulomas, related to infection; three of these had no surface epithelium and nine had partial covering of squamous epithelium. Eight specimens showed verruca acuminata, the infectious wart, usually treated by fulguration. In 13 specimens showing suburethral diverticula, there was a lining of squamous epithelium in four, transitional epithelium in two, columnar epithelium in two, and inflammatory tissue alone in five. Excision was followed by postoperative hemorrhage in one case, a temporary fistula that healed spontaneously in one, and a recurrent diverticulum in one, which was cured by reexcision.

Two suburethral cysts, lined by transitional epithelium, were excised without mishap. Carcinoma of the urethra was seen in two patients. One cancer grew very rapidly, one more slowly. Rapidity of growth may be a determining factor in the choice of irradiation or excision.

Chronic urethritis and trigonitis in women commonly appear to have a psychogenic origin. After thorough investigation, these conditions are treated better by tranquilizing drugs and approach to the emotional causal factors.

408 Heyburn Bldg. (2) (Dr. Gray).

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Thrombocytopenic Purpura.—Immune thrombocytopenic purpura due to Fuadin [antimony compound used in the treatment of parasitic infections] occurred on 2 occasions when the drug was given. Administration of plasma from this patient to a recipient who also received Fuadin produced thrombocytopenia without purpura. It is postulated that thrombocytopenic purpura . . . was due to the occurrence of a drug-antibody complex capable of destroying or agglutinating platelets and depressing megakaryocyte activity.—J. V. Rivera, H. F. Rodriguez, and E. Perez-Santiago, *The American Journal of Tropical Medicine and Hygiene*, September, 1956.

URINARY INCONTINENCE

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• *Of 132 patients who had a simple vesicourethral suspension for urinary stress incontinence, 84% could be considered completely cured. Urinary stress incontinence, considered the most commonly acquired type of female incontinence, is generally the result of birth trauma or a sequel to some form of vaginal operation. While the operative procedure described may be considered relatively simple and safe, its effectiveness depends on careful patient selectivity based on extremely detailed diagnostic procedures.*

The complaint of urinary incontinence in the female is not an infrequent one. It is a distressing complaint, especially since it frequently afflicts women who are otherwise in good general physical condition. Interest in the nature and varieties of urinary incontinence as well as in the approaches to its correction has been widespread and abundant. In recent years, for instance, much has been written about, and many operations have been devised or modified for, the correction of urinary stress incontinence. The operation, however, is yet to be found for the unfailing cure of this complaint.

Without entering into a complete discussion of the various causes of incontinence, one must be reminded that there are neurological, urologic, and psychosomatic sources as well as obstetric and gynecologic ones. Furthermore, urinary incontinence may be congenital, though more often it is acquired. This paper will be confined to the most frequently acquired type of female incontinence, that is, urinary stress incontinence. It is generally agreed that this type of loss of urinary control generally is the result of birth trauma and occasionally is a sequel to some form of vaginal operation.

Diagnosis

The diagnosis of female urinary stress incontinence is not always easy. Aside from a very searching history and an adequate general physical examination (to clude a thorough vaginal examination and a simple eurological examination), complete urinalysis, endoscopy, cystoscopy, cystometry, urethrocystography, evaluation of renal function, and any other test that seems indicated should be regularly used to determine whether one is dealing with stress incontinence. Stress incontinence is most often confused with urge incontinence. Where the two conditions coexist, it becomes obvious that the urge incontinence is to be treated before one may proceed with the correction of the other. In my experience, I have learned that a complete urinalysis, including a urine culture and endocystoscopy, is a mandatory procedure in diagnostic examination.

Finally, the urethral elevation test or so-called stress test is to be done, not only to help confirm the diagnosis of stress incontinence but also to aid in predicting the result that might be expected from a particular type of operation. Briefly, the stress test consists of filling the bladder with 250 cc. of saline solution and then having the patient cough or sneeze in the lithotomy and standing positions. If the patient really has loss of urinary control, this test will demonstrate it. After the incontinence has been confirmed, the bladder is refilled to the same capacity if necessary. Then, with two digits in the vagina, the urethra and neck of the bladder are elevated and supported behind the symphysis pubis, simulating the objective of simple vesicourethral suspension. Care must be exercised not to obstruct the urethral lumen during this maneuver by placing the fingers lateral to the urethra. Under these circumstances, the patient is asked to cough or sneeze again in the lithotomy and sometimes in the standing position, and, if she manifests no loss of urine, a probable successful outcome from the operation is predicted.

Technique

A review of the different types of operations that have been described for the correction of stress incontinence will be omitted in this presentation. However, a description of the operation of simple vesicourethral suspension published by Marshall, Krantz, and me[1] in 1949 bears repetition, since a few minor modifications have changed slightly the original technique. After the patient has been prepared for operation, a 24-F. Foley catheter with a 30-cc. balloon is inserted into the bladder and the bag inflated. The operation is usually done with the patient under general anesthesia. The patient is then placed in a slightly inclined Trendelenburg position. A suprapubic incision is made to expose the space of Retzius widely. A vertical or Pfannenstiel incision may be made through the skin. The bladder and urethra may be separated from the posterior surface of the pubis and rectus muscles down to about 1 cm. of the position of the external urethral meatus by use of light pressure, applied with a sponge on a ring forceps, on the top of the bladder and the urethra.

It should be pointed out that the suspensory attachments between these structures are found to be very delicate in the female, when compared to the strong puboprostatic ligaments of the normal male. Formerly an assistant's fingers were inserted in the vagina, to aid the operator to palpate the catheter and the balloon and thus properly identify the position of the urethra and the bladder neck. This part of the technique no longer is found to be necessary. It is recommended, however, for those who are doing the procedure the first few times. One should be cautioned to be gentle when the perivesical and periurethral tissues are pushed aside by blunt dissection, since these tissues contain many blood vessels, especially veins, and as a result, if gentleness and some care are not exercised, one may encounter a considerable amount of bleeding and oozing. Should this occur, it should be controlled by pressure.

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Read before the Joint Meeting of the Section on Obstetrics and Gynecology and the Section on Urology at the 105th Annual Meeting of the American Medical Association, Chicago, June 14, 1956.

After adequate exposure of the bladder and urethra, three sutures of 1 chromic absorbable surgical suture are placed equidistant from each other on either side of the urethra. With each one of these sutures a round needle is used to carry the suture deeply into the vaginal wall adjacent to the urethra, but not to include the lateral wall of the urethra, as was indicated in the original description of the procedure. A double bite in the vaginal wall may be taken to insure a secure hold. Then the long end of each one of these sutures may be carried by a round cutting needle and secured to the periosteum of the pubis, and whenever feasible to the cartilage of the symphysis. An effort should be made to have the position of these sutures correspond as much as possible, in order to avoid distortion and inordinate tension. Before these sutures are tied, another suture should be placed in the midline at the juncture of the urethra and the bladder neck in the same manner that the previous ones were placed. After this, they are properly identified and tied. This portion of the operation brings the urethra and bladder in close apposition to the posterior surface of the symphysis pubis and partially obliterates the space of Retzius.

Additional sutures are now placed at points lateral to the urethra where the vaginal wall is found sagging. Usually one such suture on each side suffices. More sutures are then placed in the musculature of the lateral and lower portions of the bladder and secured to the posterior surfaces of the rectus muscles. This further pulls the bladder anteriorly into the space of Retzius. The number of sutures to be used in this part of the operation is governed by the needs in each individual case. A small rubber drain is placed laterally on each side of the operative site and the abdominal wound is closed in a routine manner, with the ends of the drains brought out through the lower end of the incision. Should the lumen of the bladder or of the urethra have been accidentally penetrated during the course of the procedure, the operative field is better protected against urinary leakage by the use of the drains in the space of Retzius and by the use of chromic absorbable surgical suture.

After the completion of the operation, the 30-cc. Foley catheter is replaced by a 5-cc. one, and a gauze pack is inserted in the vagina before the patient is removed from the operating table. The pack is removed from the vagina on the following day. The suprapubic drains are usually taken out on the second postoperative day and the catheter on the fourth day. In most instances, the patient voids spontaneously after removal of the catheter. She is usually discharged from the hospital on the eighth or ninth postoperative day.

Advantages and Indications

Although it is fully realized that this technique is not the answer to all cases of urinary stress incontinence, some of its chief advantages should be mentioned. The approach is simple and the technique may be considered relatively easy. The field of operation is unobstructed and sufficiently wide to permit a full view of the superior and lateral aspects of the urethra and the neck and base of the bladder. The best indication for this procedure, in our experience, is in cases of recurrent stress incontinence where repeated standard vaginal operations have failed and where, as a result of scarring and distortion, further approach through the vaginal route is no longer feasible. The procedure may be primarily elected in elderly women in whom a major vaginal operation is not advisable but in whom the restoration of urinary control is paramount for their comfort and well-being. It may be further elected in women, particularly those of childbearing age, who complain solely of stress incontinence and who appear to have no need for vaginal plastic surgery.

Clinical Data

The clinical data that will be briefly presented are gleaned from the combined experience of myself, Marshall, and Shultis [2] with 132 patients who had a simple vesicourethral suspension for urinary stress incontinence.

Age Incidence.—The average age among these patients was 54 years. The youngest patient was 21 years of age and the oldest was 76 years.

Classification.—After the degree of incontinence was evaluated in each case, 55 cases were classified as severe or as those in which patients constantly had loss of control, 64 as moderate, and 13 as mild.

History of Previous Operations.—There were 65 patients who had had previous vaginal operations. Fifteen of these had had a total of 35 operations on the urethra or bladder for loss of urinary control. In the remainder, the operation was elected as a primary procedure. The operation was combined with total abdominal hysterectomy on six occasions and with a posterior repair on nine occasions.

Vesicourethral Suspension and Pregnancy.—In this series, four women were delivered of five babies after having had a vesicourethral suspension. One had two spontaneous deliveries and each of two had one after the operation. The fourth patient had a cesarean section, since her previous operative history included not only a vesicourethral suspension for incontinence but also a successful procedure for the closure of a vesicovaginal fistula. To date, there has been no recurrence of incontinence among these four patients after their pregnancies.

Results.—Results were classified as successes or failures. In other words, the result for any patient who was not totally relieved of incontinence, even though there might have been some improvement, was counted as a failure. The follow-up on these cases now has extended over 10 years, and only 4 of the 132 patients have been lost to follow-up over this period. The rate of immediate successes in our survey reached 88.6%. Among these there were six patients who had late recurrences of their incontinence, which reduces the over-all incidence of successful outcomes to 84%. It ought to be stated that some of the earlier patients were ill-chosen and today would not be considered desirable candidates for the operation.

Complications.—In our experience, the complications encountered until now cannot be considered serious. In approximately 75% of the cases, a transient hematuria lasting from 12 to 24 hours was noted. In four instances, periostitis pubis complicated the postoperative course, and all of these patients promptly responded to antibiotic therapy. Repeated catheterizations had to be resorted to in four patients for 7, 12, 15, and 17 days respectively. Cellulitis in the region of the incision was encountered twice. Hematomas complicated the picture on four occasions and one of these was associated with a dehiscence of the wound. In one case where nonabsorbable suture material was used, a urinary fistula ensued, which spontaneously healed by the end of three weeks. One patient developed an incisional hernia postoperatively, and this was subsequently repaired.

Morbidity.—There was one death among this group of patients. It occurred in a woman 75 years of age who died on the second postoperative day from a pulmonary embolism.

Summary

The complaint of urinary stress incontinence in the female is not rare, and the diagnosis at times is not easy. Among many of the diagnostic procedures that may be used, a complete urinalysis; endocystoscopy, including urine culture; and the urethral elevation test are mandatory in each case before operative correction may be considered. Although simple vesicourethral suspension is not a cure-all, it has earned a creditable place among many other operations that have been devised for the correction of stress incontinence. The technique is not difficult, and it is a relatively safe procedure to undertake. It is indicated best in cases where repeated vaginal operations have failed.

In over 10 years of experience with simple vesicourethral suspension, the complications have not been serious. Unless urinary control was totally restored, the result in a patient was considered a failure; it was never made worse by the operation. Finally, an overall incidence of success of 84% was achieved. As experience grows and as one becomes more selective in the choice of candidates for the operation, I feel confident that a still higher rate of success will be attained.

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COMBINATION THERAPY OF RETINOBLASTOMA WITH TRIETHYLENE MELAMINE AND RADIOTHERAPY

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• *Retinoblastoma in 50 children between the ages of 2 months and 7 years was treated by a combination of radiotherapy and triethylene melamine. This series included only cases in which the disease had not extended beyond the local area. The usual dosage of radiation was 2,400 r in air through each of two portals. The drug was given by mouth originally and later by intramuscular injection, or by instillation into the internal carotid artery, the dosage being adjusted according to the weight and hematological response of the patient. The tumor was arrested and vision preserved, as judged from subsequent observation over a period of at least six months, in 12 out of 33 children who received the drug by mouth. Arrest of tumor growth and retention of useful vision was achieved in seven of eight children who received the drug intramuscularly. The intracarotid route was used in nine far advanced cases that had been classified as "almost hopeless"; in this group the tumor was arrested and useful vision preserved in two cases. The results have been better than those obtained in the past in comparable series with radiotherapy alone. Therapeutic doses of triethylene melamine produce hematological depression, and complete blood cell and platelet counts are a necessary and useful guide to the dosage and prevention of potentially severe toxic reaction in these cases. Given by mouth, the drug produced the maximum leukopenia in about nine days; given intramuscularly, it required about half that time. The latter route is definitely preferred.*

Retinoblastoma is a uniformly fatal, progressive disease appearing most frequently in children between the ages of 6 and 24 months. The untreated tumor usually advances by direct extension along the optic nerve into the central nervous system or spreads via the blood stream to skin, skeleton, and eventually to other organs. Recently the therapy of this neoplasm has been undergoing modification and improvement, especially in regard to the techniques of radiotherapy.[1] However, the appearance in a number of instances of late hemorrhagic retinitis and the percentage of failures requiring eventual enucleation have led to the consideration of other modes of therapy.

The experimental work of Gillette and Bodenstein[2] has indicated that nitrogen mustard might have a specific effect on the proliferating retinal cells. In 1953 Woods and Kupfer[3] first reported the combination of nitrogen mustard and radiotherapy in the treatment of a patient with this disease. An attempt to evaluate the possible additive or synergistic effect of nitrogen mustard analogues and radiotherapy has been in progress since 1953 as a joint project of the departments of ophthalmology, radiotherapy, and medicine of the Columbia-Presbyterian Medical Center. The results of the study will be reported below.

Methods and Patient Material

Fifty-five patients with retinoblastoma have been treated since January, 1953, with combined radiotherapy and triethylene melamine. Of these, 50 cases will be reported, since in these therapy has been completed for at least six months to three years. With repeated examinations by an experienced ophthalmologist, the eventual outcome of therapy for this tumor is generally predictable in less than five years after completion of treatment, because of calcification and certain other characteristics noted when this tumor becomes arrested.[4]

The patients selected were those in whom adequate preliminary study disclosed that the disease had not extended beyond the local area. Adequate preliminary study included chest, skull, and orbital x-rays and skeletal x-ray survey, urinalysis, and a complete blood cell and platelet count, in addition to a careful history and physical examination. The children were generally from 6 months to 2 years of age, with the range being from 2 months to 7 years. Triethylene melamine was selected originally because it was available in a form for oral administration, in view of the difficulty of intravenous administration of nitrogen mustard in small children.

The triethylene melamine was given orally with 2 gm. of sodium bicarbonate with the patient in the fasting state, according to the method of Gellhorn,[5] and 24 hours later ocular radiotherapy was instituted. The second dose of triethylene melamine usually coincided with the last radiotherapy treatment, and the third dose was given after radiotherapy was completed but within the time period of its continued direct effect. The optimal timing of these two agents is a matter of further study at present. The dose selected at first was based on previous experience with adults and was modified subsequently according to the hematological response of the patient. At present the form for oral administration has been discarded because emesis and irregularity of absorption interfere with accuracy of dosage, especially when leukopenia or thrombopenia does not develop.

Currently, a new preparation of triethylene melamine for parenteral administration is being used. Eight patients have been treated with intramuscular injections and nine with intra-arterial injections made directly into the internal carotid artery. The preparation of triethylene melamine for intramuscular administration was given in a dosage of about 0.1 mg. per kilogram, with the patient in the fasting state, by the following routine: A 2-cc. sterile tuberculin syringe was used throughout; 5 ml. of isotonic sodium chloride solution was added to a 5-mg. bottle of triethylene melamine, which had been kept refrigerated. The solution was mixed immediately before administration. The exact amount was withdrawn (equivalent in milliliter to milligram of drug) and injected promptly intramuscularly. Temperatures were recorded every two hours. After treatment the child received nothing orally for four hours, then water or ginger ale for the next four hours, and then other clear fluids for the third four-hour period. If these were well tolerated, a full fluid diet was allowed and then a light diet, as tolerated, after an additional four hours. The patient was usually discharged about 24 to 36 hours after treatment if afebrile and not vomiting.

Results

A summary of the experience with combination therapy with use of orally given triethylene melamine and radiotherapy is presented in table 1 for the first 33 children treated. The tumor was arrested and useful vision preserved in 12, or 36%. All patients were treated, no matter how large the lesion, if it was felt that some vision could be preserved. However, it is apparent from table 1 that the best results were obtained in the group in whom medium or small-sized tumors were present. Nine of the 11 patients in this group showed favorable response, whereas only 2 of a group of 10 children with large tumors (none of whom would have been treated with x-rays prior to 1953) showed favorable responses to combination therapy.

These findings may be compared with those that have been previously reported by us with others,[6] in which 23% of 122 children treated with radiotherapy alone had the tumor arrested and useful vision preserved. Prior to 1953 the children receiving radiotherapy alone were generally given 5,600 to 8,000 r in air through each of two portals to the tumor (table 2), whereas the patients undergoing combined therapy at present usually receive only 2,400 r in air through each of two portals. In the earlier treatment group, the difference between failure and success was unrelated to the amount of radiation received. Whereas 18% of

TABLE 1.—*Combination Therapy of Retinoblastoma with Use of Radiotherapy and Triethylene Melamine Given by Oral Route*

		Involvement		Tumor Arrested				Tumor Not Controlled			
Condition	No of Cases	Bilateral	Unilateral	Good Vision	Limited Vision	No Vision	Bilateral Enucleation	Good Vision	Limited Vision	No Vision	Died
'Almost hopeless'	3	3					1			2	
Optic nerve invasion	9	7	2	1*			1†			3	4
Large tumor	10	10		1	1	1	4	1	1		1
Medium tumor	5	5		4			1				
Small tumor	6	6		5							1
Total	33	31(94%)	2(6%)	11(33%)	1(3%)	1(3%)	7(21%)	1(3%)	1(3%)	5(15%)	6(18%)

* Invasion in distal portion of nerves † Exenteration

TABLE 2.—*Combination Therapy of Retinoblastoma with Use of Radiotherapy and Triethylene Melamine Given by Intracarotid Route*

		Involvement		Tumor Arrested	Tumor Not Controlled			
Condition	No of Cases	Bilateral	Unilateral	Good Vision	Good Vision	Limited Vision	No Vision	Died
'Almost hopeless'	1	1		1				
Optic nerve invasion	5	3	2				2	3
Large tumor	2	2		1	1			
Small tumor	1	1					1	
Total	9	7(77%)	2(22%)	2(22%)	1(11%)		3(33%)	2(22%)

the children had died in the original combined treatment group in 40 months, as first reported by us with others,[6b] about 35% had died in the group treated with radiotherapy alone in 10 years. Figures 1 and 2 are reproductions of an artist's sketches of findings in the pretreatment and post-treatment phase of two successful cases of combined therapy (see legends).

Eight patients have been treated with triethylene melamine given intramuscularly. At present seven have tumor arrest with retention of useful vision and one is alive with tumor arrest but no vision. A moderate leukopenic and/or thrombopenic effect was obtained in almost all patients treated intramuscularly, whereas there were many instances in which mild or no marrow depression was observed after oral administration of triethylene melamine. The possibility that larger doses were responsible for better results in the intramuscularly treated group is under study.

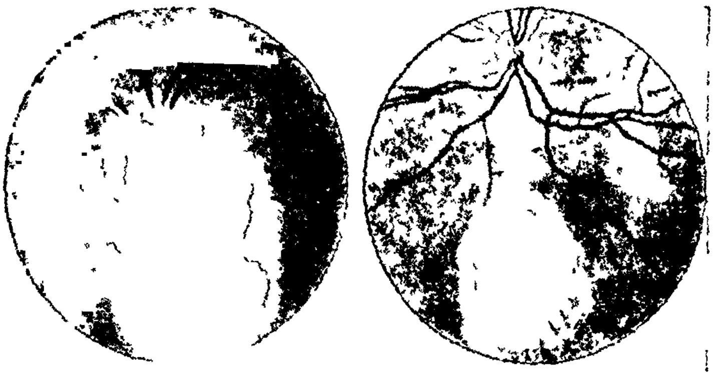

Fig. 1. (table 3, case 4).—*Left*, lesion in left eye before treatment; *right*, lesion in left eye 21 months after treatment

In an attempt to increase manyfold the amount of drug reaching the tumor, in nine instances, as mentioned above, triethylene melamine was instilled under direct operative vision into the internal carotid artery of the side corresponding to the eye to be treated. Patients were selected for this type of instillation of triethylene melamine (1) when the tumor was found to be very large but enucleation was refused by the parents, (2) when tumor cells were seen histologically at the cut end of the optic nerve at the time of enucleation (formerly an invariably fatal situation), or (3) when an orbital regrowth of tumor was present after an earlier enucleation. In addition to triethylene melamine therapy, radiotherapy was given to the eye or orbit, and if necessary orbital exenteration was performed. Table 2 summarizes the results of treatment of these "almost hopeless" cases. In this group two have had the tumor arrested and vision preserved, three have died, and an additional four apparently have active disease. Prior to 1953 these children would have been considered hopeless and would not have been treated.

The heightened local effect of the intra-arterial instillation of triethylene melamine is demonstrated by the findings in the case of a patient in whom enucleation of the right eye had revealed extensive invasion of tumor into the optic nerve. The lesion in the left eye appeared more favorable, and treatment was started with orally given triethylene melamine and radiotherapy. Soon thereafter a mass appeared in the right orbit, followed by intracranial extension. The patient had triethylene melamine instilled into the right carotid artery, and within three weeks a huge orbital mass on the injected side had almost vanished. At autopsy shortly thereafter only a hemorrhagic necrotic residue containing a small number of cells with deep staining nuclei and scanty cytoplasm remained on the right. This was in contrast to findings in the left eye, treated earlier with orally given triethylene melamine and radiotherapy, which showed viable tumor. The intra-arterial method of treatment is under further study.

Toxicity

One child in the series of 50 patients, many of whom had received four to six treatments with triethylene melamine, died of effects directly related to marrow depression (case 19, table 3). This child suffered a head injury while thrombopenia was present and subsequently died at another hospital of a subdural hematoma. In this patient leukopenia had appeared after only two days, a serious prognostic sign in our experience. When leukopenia did not occur before the fifth day, marked depression was rarely seen. Since this episode early in the study, children have received prednisone (Meticorten) and a broad-spectrum antibiotic in an empirical attempt to prevent bleeding manifestations and infection, respectively, if the platelet count fell below 50,000 per cubic millimeter and/or the white blood cell count fell below 2,000 per cubic millimeter. Prednisone was given orally in a dose of 2.5 mg. four times daily until the platelet count returned to 100,000, and the antibiotic was given until the leukocyte count returned to 3,000. Prednisone therapy was then gradually discontinued by reducing the dose in 2.5-mg. steps over a three-week period. In only one instance in the entire series was a transfusion required (case 24, table 3).

The marrow depression that may occur after triethylene melamine therapy is often a useful indicator of adequate dosage. Complete blood cell counts with platelet counts were performed two to three times weekly after treatment. In general, a moderate leukopenia of about 3,000 per cubic millimeter appeared on the fifth day after the intramuscular injection and on the fourth day after the intra-arterial instillation, indicating no significant difference between these two routes of administration. Oral therapy rarely depressed the leukocyte count to the level of 3,000 per cubic millimeter, with the low point reached generally on the ninth day, about double the time interval after parenteral administration. The platelet depression (to 100,000 or below) usually occurred later than the

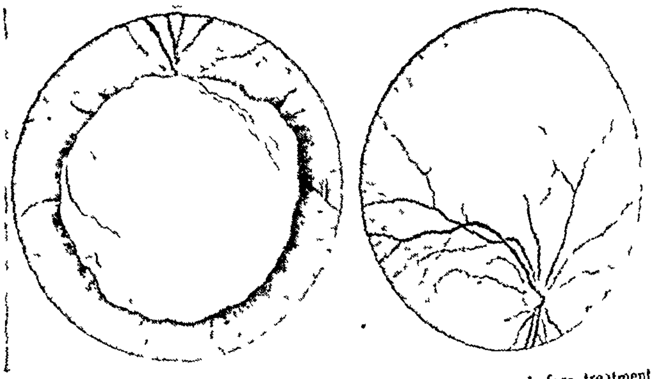

Fig. 2. (table 3, case 13).—*Left*, lesion in right eye before treatment, *right*, lesion in right eye 21 months after treatment.

TABLE 3.—*Summary of Treatment of Retinoblastoma with Triethylene Melamine Therapy and Radiotherapy*

Case No.	Age in Yr/Mo-Wt in Kg	Bilateral Tumor Present	Size of Lesion Treated	Optic Nerve Involvement	Route of Triethylene Melamine Therapy	Total Dose Mg/No. of Treatments	Duration of Triethylene Melamine Therapy Yr/Mo	Leukopenia and/or Thrombopenia: Moderate*	Leukopenia and/or Thrombopenia: Marked†	Therapeutic Results‡	Length of Follow-Up Yr/Mo.
1	2/11-16.5	Yes		Yes§	Oral	15/5	0/5			A	2/5
2	0/9-10.5	Yes	Massive		Oral	13.75/6	0/10	5		D	2/4
3	1/1-11.4	Yes	Large	Choroid	Oral	15/6	0/8			E	2/1
4	0/7-8.3	Yes	Medium		Oral	14.5/5	1/3	1		A	1/9
5	0/5-8.6	Yes	Small		Oral	15/6	1/3	1		A	1/8
6	2/8-11.5	Yes	Large		Oral	13/4	0/7	2		F	1/10
7	2/10-10.8	Yes		Yes	Oral	11/4	0/5	1		D‖	1/11
8	1/0-13.6	Yes	Massive		Oral	12/4	0/5	3		G	1/10
9	0/5-6.4	Yes	Medium		Oral	15/7	1/1	5	1	A	1/10
10	1/0-11.1	Yes	Small		Oral	15.5/5	0/8	4		A	1/4
11	2/9-13.0	Yes	Large	Choroid	Oral	15/5	0/6	4		D	1/6
12	1/5-11.1	Yes	Medium		Oral	15.5/5	0/8	3		A	1/5
13	1/2-12.2	Yes	Small		Oral	16/6	1/0	2		A	1/9
14	1/10-10.3	Yes		Yes	Oral	2.5/1	0/1			H	
15	1/2-8.6	Yes		Yes	Oral	6.5/3					
	1/9-8.9				I.A	3	0/7		1	H	
16	1/9-13.6	No		Yes	Oral	7/2					
					Nitrogen mustard, I.V.	5					
					I.A	3	0/5	1	1	H	
17	2/3-12.[illegible]	No		Yes	I.A	4/2	0/4	2	1	H	0/10
18	0/11-10	Yes	Large		Oral	8.5/3		1			
	1/4-11.4				I.M	4/2	0/7	2		D	0/9
19	0/5-8	Yes	Small	?	Oral	7.5/3					
	0/8-10				I.M	3	0/3	1	1	H¶	
20	0/10-8.65	Yes		Yes	I.A	3.25/2	0/3	2	2	G	1/0
21	1/10-9.5	Yes		Yes	Oral	17.5/6	0/7	3		G	1/5
22	0/9-12.7	Yes		Yes	Oral	10.5/4	0/5			G	1/3
23	2/6-14.5	Yes		Yes	Oral	14/4		4			
	3/0-16.5				I.M	2.5	0/6		1	G	1/1
24	0/8-9.3	Yes	Small		Oral	9/3		2	2		
	1/0-10				I.M	4.5/2	0/5	2		A	0/7
25	2/3-12.5	Yes		Yes	I.A	5/2	0/1	1		G	1/11
26	2/10-13.3	Yes	Medium		Oral	5/2	Incomplete				2/6
27	1/6-11.9	Yes	Medium		Oral	16.5/7		1			
	2/6-14.5				I.A	2	0/10	1		D	1/10
28	1/1-13	Yes	Massive		I.A	3/2	0/4	2		A	0/4
29	2/9-12.[illegible]	Yes	Large		I.M	4/2 (To date)	0/2	2		A	Under treatment
30	0/8-7.9	Yes	Small		I.M	4.6/3 (To date)	0/9	3	3	A	Under treatment
31	7/9-31.[illegible]	Yes	Large	Choroid	I.M	14/4 (To date)	0/6	4		B	Under treatment
32	0/8-9.5	Yes	Large	Choroid	I.M	6/4 (To date)	0/6	1		A	Under treatment
33	2/2-12.1	Yes	Small		Oral	17/5		1			
	3/5-14				I.A	4/2	0/7	2	1	G	0/6
34	2/10-12.7	Yes		Yes	I.A	2	0/[illegible]			H	
35	7/2-25.4	Yes	Small		Nitrogen mustard, I.V.	15/2	0/1	1		A	2/0
36	0/11-7.9	Yes	Large		Oral	17/6	0/7	2		D	1/6
37	0/7-8	Yes	Large		Oral	16.5/7		3			
	1/10-13.6				I.A	1.5	1/3	1		H	1/8
38	2/9-12.6	No		Yes	Oral	16/6	0/7			H	0/2
39	0/11-9	Yes	Large		I.A	2.8/2	0/2	2		E	0/9
40	1/4-11.8	Yes	Massive	§	Oral	14/6		2	1		
	2/4-13.4				I.A.	2	0/8			G	1/5
41	3/4-14	No		Yes	I.A	1.8		1		H	0/6
42	0/3-6.3	Yes	Large	Ciliary Body	Oral	18.5/7		2			
	2/8-14				I.M	1.5	1/4	1		D	0/7
43	3/2-15	Yes	Small		Oral	16/6	1/1	2		A	1/6
44	2/6-14.6	Yes	Large		Oral	15/5	0/8	5		B	1/4
45	4/7-18	Yes	Large		I.M	10.5/4 (To date)	0/5	2		C	Under treatment
46	3/1-14	Yes	Medium		I.M	11.75/5 (To date)	0/9	1	1	A	Under treatment
47	1/5-10.5	Yes	Large		Oral	15.5/5	0/7	2		A	1/9
48	1/8-12	Yes	Large		Oral	15.5/6	0/5	1		C	1/7
49	1/4-10	Yes	Medium		Oral	15.5/6	0/7	1		A	1/8
50	3/7-18	Yes	Large		I.M	6.8/3 (To date)	0/3	1		A	Under treatment

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* Number of instances of leukocytes below 3,000 after intramuscular administration or below 5,000 after oral administration and or platelets below 100,000 per cubic millimeter.

† Number of instances of leukocytes below 2,000 and/or platelets below 50,000 per cubic millimeter.

‡ Results A—tumor arrested, good vision; B—tumor arrested, limited vision; C—tumor arrested, no vision; D—tumor arrested, bilateral enucleation; E—tumor active, good vision; F—tumor active, limited vision; G—tumor active, no vision; and H—died

§ Invasion of distal portion of optic nerve.

‖ Exenteration

¶ Death from subdural hemorrhage after injury maximal leukopenia response, with the low point being reached after intramuscular injection on the 24th day and after intracarotid instillation on the 25th day. The additional safety factor of performing platelet counts is emphasized by the fact that the return of the platelet count to normal occurred later than with the leukocytes. Consequently additional treatment was withheld until the platelets rose above 200,000 per cubic millimeter and the leukocytes above 6,000. Nausea and vomiting occurred in about one-half of the children treated, but was either mild or easily controlled by administration of chlorpromazine. Temperature as high as 101 F (38.3 C) was noted in a few of the smaller children during the first 24 hours.

Comment

The combination of radiotherapy and triethylene melamine therapy has resulted in the apparent arrest of retinoblastoma and the retention of useful vision in 21, or 42%, of 50 children so treated. If the nine patients who received intra-arterial chemotherapy in an attempt to control an otherwise "hopeless" situation are excluded, then 19, or 46%, of 41 patients have exhibited apparent arrest of the tumor. This result has shown combination therapy to be significantly better than the method used in an earlier series [6b] in which radiotherapy alone resulted in the apparent arrest of retinoblastoma, with retention of useful vision, in 28 patients, or 23%, of 122 treated. (An additional study is now in progress in which alternate selection of patients receiving either combined therapy or radiotherapy alone is being used in order to obtain statistical information that may confirm the presumption that combination therapy seems more effective in selected cases than radiotherapy alone.)

Table 4.—*Combination Therapy of Retinoblastoma with Use of Radiotherapy and Triethylene Melamine Given by Oral and Intramuscular Route*

Size of Tumor	No.	Tumor Arrested: Vision	Tumor Arrested: No Vision	Tumor Not Controlled: Alive (Enucleation)	Tumor Not Controlled: Died
Large	15	6	2	6	1
Medium	6	5	1		
Small	8	7			1
Total	29	18(62%)	3(10%)	6(21%)	2(7%)

The group treated with radiotherapy alone received 5,600 to 8,000 r in air to the tumor, whereas the present group generally received only 2,400 r in air to the tumor in combination with triethylene melamine. Thus the hazard of a late hemorrhagic retinitis resulting in blindness was almost entirely avoided in the combined treatment group, while the results of therapy were as good or better. Furthermore, the patients in the earlier series, treated prior to 1953, generally had either small or medium-sized tumors. Since the advent of combined therapy, all patients in whom any useful vision was present have been treated, including 15 with large tumors.

The results achieved with combination therapy of patients with either small or medium-sized lesions indicate that the tumors in 12 of 14 patients, or 85%, apparently have been arrested, with retention of useful vision. Extension of the group to include all but the "almost hopeless" shows that the tumors in 18 of 29 patients, or 62%, apparently have been arrested, with retention of useful vision (table 4). Future results may prove to be better with the children receiving triethylene melamine intramuscularly, since the small group of patients treated intramuscularly to date has the highest percentage of arrested tumors (tables 1 and 3).

The intramuscular dose that we have selected as optimal is approximately 0.1 mg. per kilogram. Because of the variation in individual sensitivity, subsequent therapy in each patient is based on the initial hematological response. The effective intramuscular dose was approximately one-third to one-half the oral dose, as has been previously reported by Karnofsky.[7]

The total dose employed has been empirical, with an average course of 15 mg. orally or 6 to 10 mg. intramuscularly extended over a 6-to-12-month period. These young children apparently tolerate much larger doses than adults, since the recommended parenteral dose of triethylene melamine in adults is only 6 to 12 mg.

Of interest is the finding that additional chemotherapy in these children with normal bone marrow may have a lessened effect on marrow activity as treatment continues, possibly indicating the presence of an adaptive mechanism in normal marrow. This situation differs sharply from that seen in patients with Hodgkin's disease or other lymphomas, since in these patients the marrow seems less able to cope with additional courses of mustard-like agents as the disease progresses.

The combination of radiotherapy and chemotherapy in treatment of tumors has many theoretical bases. Research by Goldberg and Schoenbach,[8] and by Timmes, Haddow, and others of their group[9] have indicated that the effect of these agents is apparently at different points on the chromosome of the dividing nucleus. If such is the case, then a synergistic action is a possibility.

A concentration of these children with a rare tumor at one medical center provides the chemotherapist with a unique situation. In addition one is dealing with an easily visible, local, and circumscribed tumor, magnified 16 times by the ophthalmoscope, so that combination therapy can be better evaluated than is generally possible in Hodgkin's disease, lymphosarcoma, or other epithelial tumors. Since retinoblastoma is an unusual cancer with a strong clinical resemblance to the lymphomas in its response to radiotherapy and the alkylating agents, one may have here a pilot-type study in which to observe the effects of combined therapy.

Summary

Because of the possibility of synergism between radiotherapy and triethylene melamine therapy, a study was commenced in January, 1953, at the Institute of Ophthalmology and the Columbia-Presbyterian Medical Center in which 50 children with retinoblastoma received combined therapy. This combination appeared to be both feasible and apparently successful in arresting retinoblastoma in a significant proportion of children with early disease. It was found that triethylene melamine could be safely administered to children in doses proportionately larger than those given to adults and that the route of choice was intramuscular.

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This study was supported by a grant from the Dunlevy Milbank Foundation, Inc

Virginia Pampellonne gave technical assistance in this study

The prednisone used in this study was supplied as Meticorten by the Schering Corporation, Bloomfield, N J

The preparation of triethylene melamine for parenteral administration was supplied by Dr. James Ruegsegger, Lederle Laboratories Division, American Cyanamid Company, Pearl River, N Y.

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DUCK-EMBRYO RABIES VACCINE

STUDY OF FIXED VIRUS VACCINE GROWN IN EMBRYONATED DUCK EGGS AND KILLED WITH BETA-PROPIOLACTONE (BPL)

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• *Improvements in the methods of immunizing against rabies are needed because neuroparalytic accidents are known to have occurred following the use of present methods. The use of embryonated duck eggs in place of rabbit brain for propagating the virus eliminates the myelin, which has been suspected of contributing to the nervous complications. The animal experiments here described showed that duck-embryo rabies vaccine could be killed by dilutions of beta-propiolactone not exceeding 1:4,000. Killed under these conditions, the virus was shown to be antigenic in mice. Detectable antibody appeared between 7 and 10 days after the first inoculation and continued to be present on the 15th and 30th days In treating bites of rabid animals, antibody must be made to appear as early as possible. The absence of brain tissue in this preparation has distinct advantages*

The occurrence of neuroparalytic accidents during rabies prophylaxis has been an ever-present hazard to successful treatment. Recent figures indicate that these accidents occur approximately once in 500 to 600 treatments.[1] Conventional antirabies vaccine propagated in rabbit brain contains myelin, which has been implicated as the factor causing central-nervous-system complications.[2] Alternative methods of vaccine preparation include (*a*) purification of brain vaccine or (*b*) growth of the virus on non-nervous tissue. We have found, in following the latter direction, that embryonated duck eggs suffice for growing fixed rabies virus.[3] Furthermore, the vaccine produced by this method is free of neuroparalytic factors, as determined by adjuvant tests in guinea pigs.[4]

We have recently described the use of embryonated duck-egg antirabies vaccine in humans.[5] One-year-old freeze-dried attenuated virus vaccine was used. The antibody response in this study was quite satisfactory, being both early in appearance and present in a great proportion of patients studied. However, it appeared prudent to kill the virus used in this vaccine providing it would maintain adequate antigenicity. This was accomplished by the use of beta-propiolactone (BPL). This report concerns laboratory and clinical aspects of beta-propiolactone–killed rabies vaccine.

Laboratory Studies

Virucidal Action of Beta-Propiolactone.—Doubled dilutions of beta-propiolactone were added to a series of six 100-ml. amounts of virus suspension. Final concentrations of beta-propiolactone in the virus suspension were from 1:1,000 to 1:32,000. After refrigeration of the suspension at 4 C for 24 hours, acidification brought about by breakdown of beta-propiolactone was corrected. Decimal dilutions of each virus suspension were injected intracerebrally into groups of five mice to determine the titer, if any, of live virus in each preparation. Untreated virus was also employed as a control. All virucidal tests were conducted under refrigeration, due to the lability of the virus at incubator temperature.

It is evident (table 1) that concentrations of beta-propiolactone of 1:1,000, 1:2,000, and 1:4,000 killed embryonated duck-egg fixed virus. The 1:8,000 to 1:32,000 concentrations of beta-propiolactone failed to do so. In a separate study (not shown) it was found that a 1:6,000 concentration of beta-propiolactone also was effective in killing the virus. Thus it was demonstrated that preparation of killed antirabies vaccine could be attempted with concentrations of beta-propiolactone up to 1:4,000 but not with concentrations of 1:8,000 or weaker.

From the Lilly Laboratory for Clinical Research, Indianapolis General Hospital, and the Lilly Research Laboratories

Immunizing Potency.—Four of the suspensions described above were next tested as antirabies vaccines in official tests of the National Institutes of Health[6] in white mice. The NIH standard vaccine was used as a control. It was observed (table 2) that the three strongest concentrations of beta-propiolactone studied were virucidal and immunized mice; however, the best immunizing action was secured with the weakest virucidal concentration of beta-propiolactone (1:4,000). The stronger concentrations were less antigenic.

TABLE 1.—*Virucidal Action of Beta-Propiolactone in Duck-Embryo Suspensions**

Virus Dilutions	Dilutions of Beta-Propiolactone						
	1:1,000	1:2,000	1:4,000	1:8,000	1:16,000	1:32,000	Control
10^{-1}	4/4	5/5	5/5	2/5	0/5	0/5	0/5
10^{-2}	5/5	5/5	5/5	5/5	3/5	0/5	0/5
10^{-3}	5/5						0/5
10^{-4}	5/5						0/5
10^{-5}							0/5
10^{-6}							2/5
							4/5

* Results given as ratio of mice surviving to mice injected. Mice were inoculated intracerebrally with suspension of virus and beta-propiolactone. Concentrations of beta-propiolactone up to 1:4,000 successfully inactivated strongest dilution of rabies virus suspension.

Consistency of Potency.—A series of batches of killed vaccine was then prepared with beta-propiolactone. None contained live virus, as evidenced by intracerebral injection of the vaccines into white mice. All batches, or lots, passed the NIH safety tests,[6] which included single subcutaneous injections of 0.25 ml. into white mice and single subcutaneous injections of 2.5 ml. into guinea pigs. The potency of these vaccines, when tested according to official NIH methods,[6] is indicated in table 3. All lots of this vaccine were much better than the standard control vaccine. Lot 698C was made with 1:2,000 concentrations of beta-propiolactone and the rest with 1:4,000 concentrations. The latter concentration was made routine on all succeeding batches.

Heat Stability.—Several lots of the beta-propiolactone-killed vaccine were subjected to heating at 37 C for periods of two or four weeks. Table 4 shows potency determinations of these various lots both before and after the periods of heating. It is observed that all of the vaccines are considerably better than the control vaccine even after four weeks of heating.

Antibody Response in Monkeys.—Fourteen daily doses of vaccine were given to each of four cynomolgus monkeys. Vaccine from lots 696 and 703 was used (tables 3 and 4). Standard serum-virus neutralization tests[7] were conducted in mice with use of 0, 15, 30, and 60 day serum specimens drawn from the monkeys. Antibody titers were computed by the method of Reed and Muench.[8] The series of injections was uneventful, and antibody response was good (table 5).

TABLE 2.—*Effect of Beta-Propiolactone on Antigenic Potency of Duck-Embryo Rabies Vaccine*

Concentration of Beta-Propiolactone*	Virus Viability	Potency† of Vaccine
1:1,000	Killed	0.55
1:2,000	Killed	1.25
1:4,000	Killed	3.28
1:8,000	Living	5.79

* Beta-propiolactone in concentrations of 1:4,000 produced the most immunizing potency with the least amount of damage to the killed virus vaccine.

† Times better than standard vaccine of National Institutes of Health.

Observations.—It is apparent that the use of beta-propiolactone in 1:4,000 concentrations is regularly successful in killing duck-embryo fixed rabies virus. The killed-virus vaccine made in this manner also acted as an effective antirabies vaccine, as judged by NIH mouse-immunization tests. It also appeared that the vaccine could withstand at least a moderate amount of poor storage conditions such as might be encountered in clinical use. Cynomolgus monkeys were effectively immunized by 14 daily injections without untoward after-effects, indicating possible clinical adaptability of the vaccine.

Clinical Studies

Clinical response to the vaccine was studied in 32 male volunteers. None had a history of allergies or prior antirabies-vaccine therapy. Twenty-one complete courses of 14 injections of vaccine were given. Also, 7 daily inoculations were given to six subjects, two of whom were originally scheduled to receive 14 injections. One person received six of seven inoculations, the seventh being omitted due to reaction. Four individuals were dropped from the study at its onset, three at their own request and one due to acute intercurrent illness. Blood specimens were obtained from all subjects prior to the first vaccination and again on the 10th, 15th, and 30th day after the first inoculation. In addition, the five individuals receiving a total of seven inoculations had a seventh-day bleeding. The entire group was divided into three subgroups, each of which received a different batch of vaccine (group A received lot 703; group B, lot 710; and group C, lot 712). Injections were made subcutaneously on the abdomen at a different site each day. The patients were checked daily for local or systemic reactions.

TABLE 3.—*Consistency of Potency of Beta-Propiolactone-Killed Duck-Embryo Rabies Vaccine*

Lot	Potency*	Lot	Potency	Lot	Potency
689-C	1.2	698-B	2.6	710	3.5
689-D	3.2	703	3.0	712	2.4
696	3.3	706	4.7	714	2.4

* Times better than standard vaccine of National Institutes of Health

Reactions to Treatment.—Two individuals were not given the entire series of 14 injections due to the occurrence of local induration severe enough to warrant discontinuation of an elective procedure. One other subject who was originally scheduled for seven injections developed chills, fever, and malaise after injection number six, and use of the vaccine was discontinued. A transitory stinging sensation, usually lasting no longer than a minute or two, was noted by all subjects at the time of injection. Tenderness at the injection site developed in a majority of patients, lasting from 24 to 72 hours. This tenderness was not incapacitating and was not considered to be a major problem.

Erythema was observed in about one-half of the individuals, the great majority of instances being sporadic in onset. Four subjects exhibited consistent erythema with each injection, the erythema being more severe as the sixth and seventh injections were given. Induration of varying degrees was noted in several subjects. Again, it was sporadic in onset but tended to be more common during the middle third of the treatment. Three individuals, all of whom had induration, also exhibited transitory regional lymphadenopathy. The local reactions to the vaccine did not appear to be as frequent as those seen when phenolized vaccine of brain origin is administered.

TABLE 4.—*Heat Stability of Duck-Embryo Rabies Vaccine Killed with Beta-Propiolactone*

Lot	Potency* Before Heating	2 Wk. at 37 C	4 Wk. at 37 C
689 D	3.28	3.96	1.87
696	3.34	1.75	3.02
703	3.08	5.06	10.00
710	3.5	2.56	3.61
712	2.44	2.43	2.26
714	2.41	4.49	1.76
722	2.24	6.89	5.96

* Times better than standard vaccine of National Institutes of Health.

Systemic Reactions.—One subject in this series developed fever, chills, anorexia, and malaise 14 hours after receiving the sixth of seven injections. It was thought that the illness represented a reaction to a foreign protein, and administration of the vaccine was discontinued. Recovery was uneventful. The patient recalled that he had had the same type of reaction to influenza vaccine 11 years previously.

Development of Virus-Neutralizing Antibodies.—All serums were studied for antibody to rabies. Titers of antibody concentration were based on standard bioassay procedures in which 100 L.D.$_{50}$ of challenge virus and 0.03 ml. of serum in varying dilutions were inoculated intracerebrally into six mice per each serum dilution.[7] The titers (table 6) were expressed as the reciprocal of the serum dilution needed to protect half the mice. In the group receiving 14 injections, all had developed antibody by the 10th day after the first injection. Antibody continued to be present on the 15th and 30th days. Only one of the group receiving seven inoculations had demonstrable antibody on the 7th day, although five of six had antibody on the 10th day. *It is interesting to note that the individual having the systemic reaction after the sixth injection had a good antibody response on the seventh day.* No differences were seen between the lots of vaccine used, either in the time of onset of antibody response or in the height of the titers. It is apparent that detectable antibody appears between 7 and 10 days after the first inoculation. No correlation could be established between the degree of local reaction and the height of antibody response in this study.

TABLE 5.—*Antibody Response in Cynomolgus Monkeys Receiving Duck-Embryo Rabies Vaccine**

Monkey	Lot	Day No. 1	15	30	60
434	696	0	12	85	25
415	696	0	64	57	23
416	703	0	83	74	12
417	703	0	12	10	10

* Antibody titers expressed as reciprocal of serum dilution saving half the mice as determined by the method of Reed and Muench.[8]

Comment

It is obvious that a prime necessity in treating bites of rabid animals is the early appearance of antibody. This is especially true if the bites are on the face and neck or if there has been massive inoculation of street virus into the wound. The use of hyperimmune serum will no doubt add to the effectiveness of treatment of these bites. It still remains, however, that early formation of active antibodies plays a very important part in prevention of rabies in humans. Rabies vaccine of duck-embryo origin produced antibodies in all subjects within 10 days. There did not appear to be a variation in antigenicity between the lots tested clinically, and the results correlate closely with those observed in tests on animals. From this it would appear that tests on animals are sufficient to establish the antigenic potency of the vaccine. The absence of brain tissue in this preparation has distinct advantages. Neuroparalytic accidents should be materially reduced in frequency if not completely eliminated. This may help the physician in solving the distressing problem of whether to give a course of vaccine to questionably exposed patients.

TABLE 6.—*Serum-Virus Neutralizing Titers in Human Subjects Injected with Beta-Propiolactone–Killed Duck-Embryo Rabies Vaccine*

Vaccine Lot	Doses, No.	Subject	Antibody Titer* on Indicated Day† After First Inoculation 7	10	15	30
703	14	A-1		16.0	22	32
	14	A-2		<4	10.2	17
	14	A-3		7.2	8	14
	14	A-4		<4	10.5	22
	14	A-7		4.5	21	10.7
	14	A-8		6.4	21	27
	14	A-9		4.0	8	<4
	14	A-10		<4	8.7	76
710	14	B-1		5.4	8.7	11
	14	B-2		5.0	12	4
	14	B-3		<4	7	5.8
	14	B-4		4.8	22.8	20
	14	B-5		12	6	ND
	14	B-6		31	11.8	28
	14	B-9		<4	7.2	ND
712	14	C-1		8.7	4	84
	14	C-2		8.5	19	64
	14	C-3		7.2	3.3	ND
	14	C-4		12	18	ND
	14	C-6		8.7	6.6	10
	14	C-9		16	7	54
703	7	A-11	0	8	11.5	6
703	7	A-12	<4	4.4	4	25.2
710	7	B-10	ND‡	4	6.6	0
710	7	B-11	0	0	0	5.2
710	7	B-12	0	4.4	10	10
722	7	C-5	ND	9	10.9	45.4
712	6	C-8	7.1	43.4	140	52

* Antibody titer expressed as reciprocal of serum dilution protecting half the mice, as calculated by method of Reed and Muench.[8] Titers of <4 indicate immunologic response in which some mice lived in test, but too few to give 1:4 titer.

† Zero day titers 0 in all cases.

‡ ND = not done.

As this vaccine contains foreign protein, one must expect to see the development of local sensitivity in some individuals, even though embryonic tissue is poorly antigenic. The fact that 14 injections are given increases the chance of sensitivity occurring. That it has not occurred in a greater number of subjects has been gratifying. Systemic reactions to foreign protein also must be anticipated in a small percentage of individuals. Since there is a greater incidence of allergic reactions in subjects with allergic histories, one should be cautious in the use of this vaccine in these individuals. This is especially true if the allergy is to chicken-egg albumin.

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THE ENIGMA OF CAUSE OF DEATH

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• *The causation of a given death is always multiple, so that the necessity of selecting a single cause for purposes of tabulation has become a distressing problem. The solution depends on the purpose for which the information is to be used. For the purposes of preventive medicine the single cause of death hitherto given has been very useful, but it would be even more valuable to indicate all those terminal morbidity conditions that meet desirable standards in defining important diseases. This would also relieve the physician of the unwelcome task of designating the dominant cause unless he wishes to do so by underscoring one.*

However strong may be our defenses against becoming victims of the dramatic statement, whether by propagandist, preacher, or politician, we are nevertheless enticed by its stirring of emotion and may use it on occasion to achieve a purpose when reason alone seems insufficient. The inadequacy of man's reason to cope fully with the problems of intimate death is a matter of common observation, and the power of emotion to bridge those voids is traditionally exploited through dramatic expression.

There seems to be a substantial carry-over from this emotional reaction to death as a personal experience to the more objective contemplation of death in general. Assertions that selected diseases are the "great killers of mankind" are common in high places. National societies promoting campaigns for funds to study those diseases contend for each death to be assigned to the disease of their special interest; thus will their claims for priority in charitable donation gain the desired weight provided by statistical evidence. Vital statisticians routinely respond in such ways as fall within their province to "fix the blame" or, in more formal language, to secure with scientific accuracy, from the medical profession, coroners, or others, a specification of the "cause" of each death. Pursuit of this objective is certainly laudable from all conventional viewpoints, but in so conforming one may become a victim of habit rather than an alert pursuer of well-reasoned objectives.

Public health workers are marshalled as forces for the preservation of good health in their respective communities through community action. Maintaining health calls for quick remedial action with respect to any defection, and most certainly before death forecloses all possibility of change. Morbidity is the prime interest, the challenge to action; mortality is merely a measure of defeat. We may appropriately mourn the dead, but let it be only in search of better means to protect the living.

In most instances, medical certification of cause of death has been vigorously sought because of conviction that the death certificate should help to define the morbidity problem. Good morbidity data of complete community coverage have not been available from other sources. If such data were readily available, our interest in cause-of-death certifications would surely vanish. But certainly no statistician worthy of his salt is going to accept even the best mortality records as other than a grossly biased sample of morbidity conditions in a total community.

Concepts of Cause of Death

It is a false proposition that each death is a response to a single cause. Of this we are well aware. Admission of multiple causation for each death is tacit in the certificate itself. We have long striven for entry of a sequence of causes rather than a single cause. As a result of this, the selection of one cause for tabulation purposes has itself become a major problem for us, leading to much juggling of terms, rules, and instructions, to the distress of the medical profession as well as the statisticians. Efforts in recent years to solve the problems of tabulation and interpretation of assignment of multiple causes represent an attack on a basic problem and clearly indicate that causation of death is not considered singular.

Cause is defined by common understanding as "that which produces an effect"; or, more cautiously, as "the group of circumstances that must precede and that invariably result in an effect." These are common dictionary forms of definition. There is ample testimony in the writings of philosophers and scientists alike, from at least the time of Aristotle onward, that assignment of cause is a metaphysical indulgence and beyond the scope of scientific undertaking. This problem has had some of its best emphasis in the work of biometricians. Two founders of the biometric school have contributed notably to clarification of the causa-

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tion issue. Francis Galton's accomplishment in providing a measure of incomplete association is well known. Too often, in disputation of the merit of his technique, we lose sight of the broader concepts his work opened to our view. His book "Natural Inheritance"[1] tremendously impressed a much younger scholar of high attainment in law, mathematics, and the sciences, Karl Pearson. Analysis of the foundations of scientific reasoning had been absorbing much of the young man's attention and led to another notable book, "The Grammar of Science," which gave considerable attention to the subject of causation.[2] Close companionship of these two men in the following years, with considerable fusion of their ideas a natural product of the meeting of their minds in repeated discussion, led to a synthesis of their thinking on the subjects of correlation and causation, to which each had contributed so much independently.

Pearson's biography[3] of his close friend gives clear definition of their viewpoint in a familiar statistical form worthy of rather full quotation here:

> . . . correlation . . . was to replace not only in the minds of many of us the old category of causation, but deeply to influence our outlook on the universe. The concept of causation—unlimitedly profitable to the physicist—began to crumble to pieces. In no case was B simply and wholly caused by A, nor indeed by C, D, E and F as well! It was really possible to go on increasing the number of contributory causes, until they might involve all the factors of the universe. . . . Henceforward the philosophical view of the universe was to be that of a correlated system of variates, approaching but by no means reaching perfect correlation, i. e. absolute causality, even in the group of phenomena termed physical.

Lest there be any tendency to regard this sort of thinking as outmoded, may I quote from a recent work of J. Robert Oppenheimer.[4] He writes thus of the new physics: "This is a very different view of reality from Newton's giant machine. It is not causal; there is no complete causal determination of the future on the basis of available knowledge of the present . . . every observation on a system reveals some new knowledge as to what its state is that did not exist before, and could not by analysis and mathematical computation have been obtained."

Complexity of Cause

What is the implication of all this for our problem of cause of death? By way of introduction to this, I would ask indulgence in considering first a simple illustration not involving health. Boys are at play in an open lot beside a house, active in a game simulating baseball. A powerful swing of the bat fails to make contact with the ball in the proper manner, and the ball spins wide of the intended course to come to rest within one of the rooms of the house, leaving a shattered pane of glass as vignette to its flight. The owner of the house, irate if not irrational in his questioning, demands to know who broke the glass, so that responsibility for its replacement may be clearly attached. To him the 'cause" of the broken pane is to be determined with one objective in view—satisfaction of his just claim for damages through assignment of responsibility to a source from which payment may be expected. But did the boy at bat break the pane of glass, as many would chorus in support of an obvious argument? The ball? Did not the pitcher play a part? And also the circumstances that led to selection of that place to play in, and the countless number of antecedents throughout past time (including all ancestors) that led to those circumstances? An articulate ball in turn could well protest that it alone did not break the glass—just as my child comments on milk flooding outward on the tablecloth from her overturned glass, "It spilled!"

It is clear that we can wrangle indefinitely about this matter of causation in specific illustrations. But is it not also clear that all observations are elements in sequences of events from deep in the past into an indeterminate future? Of the facts of broken glass or spilled milk there is no doubt. And that each was the inevitable outcome of the long line of antecedents that preceded it, constituting the causal system, we feel confident there is also no doubt. Are not causes just the members, infinite in number, of causal systems that in their totality are beyond our comprehension? We may select from such a system an individual factor and, in assigning to it an importance that is suitable to our reasoning of the moment, claim it to be the cause of the result. This is clearly arbitrary selection. We habitually prescribe that all else outside those members of the system that we choose to consider shall be deemed extraneous for purposes of discussion. In this sense a weight added to one side of a balance may be considered the sole cause of a subsequent movement in the balance. This is causation in the Newtonian sense. Its justification is implicit in the simplicity of the situation studied.

A question of major concern to us just now is whether we can establish sufficient analogy between such simple situations and the very complex one of establishing cause of death. It may help us here to consider life as like a functioning motor, self-regulating and capable of many internal compensations, vulnerable to external attack and internal decay. Actuarial tables define its expected duration under the hazards characteristics of specific time periods. Any predominant factor or incident of outstanding importance leading to unexpectedly early breakdown of this machine may be accepted by us all, without conflict of opinion, as an appropriate cause to which the death (complete and irrevocable stillness in the motor) should be assigned. Accidents and acute communicable diseases come quickly to mind as illustrations of such factors. Other elements playing their normal roles in the complete causal system are readily accepted as being relatively unimportant and are dismissed from consideration. The arbitrary designation of one cause is nevertheless an overriding simplification. Its acceptance is made possible through unanimous agreement that it serves the purpose for which knowledge of cause is required, all other causal factors are in this light trivial.

Shift the disease from acute to chronic or the accident to suicide, for instance, and it may become extremely difficult any longer to get anything approaching unanimity of agreement as to what is now to be accepted as the responsible cause. Those advanced in years are not infrequently known to be host to more than one disease condition, each of which in some degree impairs ability to function. Death finally comes, as it must to all, and the necessity of specifying a cause on the death certificate initiates somewhat of a scramble. Not infrequently what appeared to be a rather clear-cut syndrome of clinical symptoms, giving the internist complete confidence in what he would assign as the cause of death, fails to jibe with findings at autopsy. How often it is true that the pathologist would insist on some other entry in the medical certification of cause of death, if that document were not already completed and filed out of his reach.

Let us consider for a moment a specific case. A person is bothered in childhood by undiagnosed rheumatic fever, but he recovers and goes on into adult life with a resultant heart defect. The latter is not serious enough to come to medical attention until hospitalization for tuberculosis leads to its discovery. In the course of time his tuberculosis is brought under control, and he is released to a new pattern of "normal activity." Some years later he is one of the victims in an automobile accident in which he suffers trauma, considerable laceration, and seemingly serious loss of blood. Death shortly after arriving at the hospital results in certification of accidental death. But autopsy leads to a pathologist's verdict that the diseased condition of the heart was the primary culprit in this death. The pathologist also discovers cancer of the bladder that, in a relatively short period of time, would undoubtedly have led to death if not caught and successfully treated. The tuberculosis does not seem to play a role in the death and is disregarded.

We may all agree that the outstanding incident among the antecedents to death in this particular case was the automobile accident and that the death should be assigned to the appropriate subclassification on the list of accidental deaths, the strain on the heart being considered as a by-product of the accident. Undoubtedly many interests will feel well satisfied by this procedure. From the point of view of health interests, however, the accident is no more than an incident; it belongs in the category of a "last straw that breaks the camel's back." Any fight among various societies for this death as belonging to their propaganda campaigns is justifiable; the record belongs in a very real sense to every one of them. The body is certainly part of the wreckage of an accident; it is also mute testimony to the wastage of rheumatic fever and heart disease, tuberculosis, and cancer. Important information on health is lost by not assigning the case to each disease category to which it properly belongs, not as a death but as an impoverished body recently alive.

The difference between this sort of situation and that of the acute communicable diseases is not fundamentally that deaths are separable into two categories with respect to causation—the simple and the complex; it is fundamentally a contrast in the relative ease with which we can secure unanimity of agreement in selecting one item out of a causal system as being the important one for the purpose in view. Let us emphasize those last words: for the purpose in view.

Effective Use of Knowledge

What is the purpose behind selection of cause of death? The appropriate answer to this question must inevitably be colored by the viewpoint of the respondent. A lawyer will think of legal reasons; an insurance company executive would consider first the obligations that the company has undertaken and possible exceptions that must be considered. Members of the health professions will have in mind the picture of morbidity in the population that they are attempting to serve. One thing will be common to all efforts to answer the question: an attempt to select the most important causal factor from the point of view of the respondent.

Our responsibilities in public health necessitate our knowing as much as possible of the total morbidity picture in each community that we serve. The medical certification of cause of death contributes to that knowledge. Effective use of that information is surely the primary justification for securing it. When study of the prevalence of disease is the task to which we claim dedication, it is most certainly wasteful of opportunity to allow ourselves to become involved in misleading argument about single cause-of-death selections. The prevalence of disease in a community will not be measured by selecting one only from these attendants at the end of life's run. We would like to have the complete morbidity picture for the whole of each life story as it unfolds, but means are not available to us for getting that. We accept the death story as an available fragment for what it may be worth with respect to those who remain.

Passing of the era of acute communicable diseases as major killers in the United States has already had a very substantial impact upon our programs in public health. We have instituted many changes of activity in an effort to meet an altered balance of needs. Some of these changes may prove to have been impulsive and taken too early. But certainly we must turn attention to deeper study of the endemiology of chronic disease. And in that connection especially, I am sure we should benefit from thought concerning the fundamental nature of causation in relation to death, and our basic reasons for seeking causes in this connection.

A Postlude

In closing this discussion I would like to anticipate a very few of the questions that must follow as a natural sequel:

1. Tabulations of deaths by specific causes have been very useful in the past. Are they to be abandoned now? Answer: Not at all. Indeed the tabulations should be extended to cover all entries on the medical certification of cause of death that meet desirable standards in defining important diseases. But certainly the term "specific causes of death" should be replaced by a more realistic term such as "terminal morbidity conditions." Perhaps a new term like "conterminous morbidity" might arise.

2. Should use of death rates specifying a cause be continued in the present form? Answer: Preferably not, even though the sophisticated may not abuse the misleading title. But for all, including this elite group, we should have a new class of rates defining proportionate morbidity at time of death. Under this title would be defined the relative frequency with which diagnosed heart disease, cancer, tuberculosis, cerebral accident, and each other causal entity of sufficient importance to receive attention appeared among those

deceased. These rates would be highly informative, covering prevalence of disease prior to decease far better than death rates specifying a cause can possibly do. It would be most important to have such rates specific for homogeneous population groups, especially by age.

3. What changes would seem desirable within the medical certification portion of the death certificate? Answer: A careful revision of wording to win better cooperation from the medical profession. The physician should be encouraged to report disease, in the detection and treatment of which his competence is acknowledged and his aid has been sought. His assistance would be given accordingly. Noncooperation to the point of antagonism is risked by superimposition on him of the unwelcome role of seer in the metaphysics of causation. We should remove all obligation to indicate a single cause for tabulation purposes. Selection of a dominant cause to which the physician would give emphasis should be voluntary, indicated perhaps by an underscore. Perhaps our vital statisticians may reconsider past decisions on this in a new light. Perhaps also business interests that occasionally pin their operations to single causes of death will reconsider the wisdom of undertakings based on vague definitions that may promote falsity.

18 E. Division St., Chicago 10.

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CLINICAL NOTES

THERAPEUTIC ASSAY OF TOPICALLY APPLIED PREDNISOLONE ALCOHOL IN SELECTED DERMATOSES

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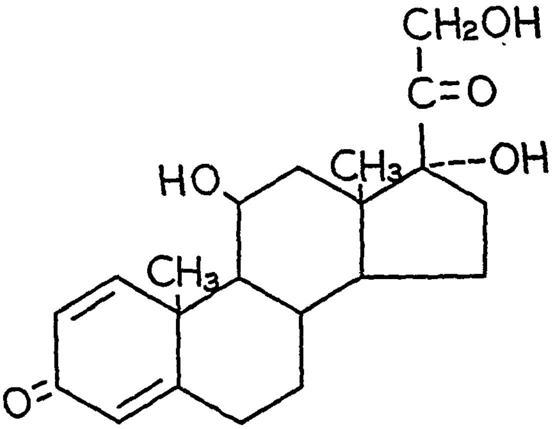
Prednisolone alcohol (Meticortelone) is a synthetic crystalline steroid with the following structural formula:



Its structure differs from that of hydrocortisone free alcohol by the presence of a double bond between C_1 and C_2. In a recent study of the effects of orally administered prednisolone, Bunim, Pechet, and Bollet[1] reported prednisolone to be approximately two to three times as effective as hydrocortisone as an antiarthritic and anti-inflammatory agent, yet its use was unaccompanied by an increase in the severity of undesirable side-effects. Goldman, Flatt, and Baskett[2] similarly found prednisolone to be more effective than hydrocortisone when administered orally in various dermatoses. Their studies indicated that prednisolone was four to five times as effective, dosage for dosage, as hydrocortisone. Since both hydrocortisone acetate and hydrocortisone free alcohol have been reported to be of value in the topical therapy of various dermatoses and to be of equal therapeutic value in equal concentrations,[3] it was thought worthwhile to compare the clinical effect of topically applied prednisolone alcohol with that of hydrocortisone free alcohol. In this way, it could be determined whether prednisolone was more effective than hydrocortisone as a topically applied medicament.

Preliminary Study

In a preliminary study, 20 patients with various dermatoses were treated by the simultaneous paired comparison method with ointments containing prednisolone alcohol (either 0.25% or 0.5%) in a white petrolatum base applied to one of two symmetrically situated areas and an ointment containing hydrocortisone free alcohol (1%) in a water-washable base applied to the other. In 14 of the 20 cases, the prednisolone alcohol in both the 0.25% and 0.5% concentrations proved to be more effective than, or as effective as, the hydrocortisone free alcohol, with the 0.5% concentration being the more effective of the two. Although this preliminary study indicated that prednisolone was of distinct value when topically applied, the fact that the prednisolone and the hydrocortisone were incorporated in different bases might have accounted for the difference in their therapeutic efficacy. The results, however, were promising enough to warrant further comparative studies, with use of identical vehicles.

Results

The present study is an attempt to compare the effectiveness of prednisolone alcohol and hydrocortisone free alcohol, with the factor of different ointment bases eliminated. It is divided into two parts; in the first part, the clinical effectiveness of a topically applied preparation of prednisolone alcohol (0.5%) (Meti-Derm) in a water-washable base (Procutan) was compared with that of hydrocortisone free alcohol (1%) (Cortifan) in the same base. A total of 137 patients were treated with these two preparations. The 16 dermatoses listed in table 1 were represented in this group of patients.

Whenever possible, the preparations were assayed by the simultaneous paired comparison method, i. e., the simultaneous application of the prednisolone alcohol (0.5%) cream to one of two symmetrically situated areas or lesions and the hydrocortisone free alcohol (1%) cream to the other. Patients were given adequate amounts of each of the preparations, which were clearly labeled as to both the site of the application and the frequency of applications (three to four times daily). Treatment periods varied from four days to eight weeks, the average being two to three weeks. Patients were observed at approximately weekly intervals for evaluation of both subjective and objective improvement.

The results of this portion of the study are given in table 1. It will be noted from this table that it was possible to carry out the simultaneous paired comparison method in 128 of the 137 cases. Treatment with the prednisolone alcohol (0.5%) cream was more effective than, or equally effective as, with the hydrocortisone free alcohol (1%) cream in 99 out of 128 cases. In nine cases it was not feasible to carry out a simultaneous paired comparison because of the body areas involved. These patients were treated with the prednisolone cream only. In eight of these the prednisolone produced a definite marked improvement, and in only one case did it fail to produce any improvement.

In an effort to determine if any of the therapeutic effectiveness of the prednisolone was due to the water-washable base itself, 24 patients were treated by the use of the simultanous paired comparison method, with the prednisolone alcohol (0.5%) cream administered to one area and a placebo water-washable base used on a symmetrically situated area. This formed the second part of the study, and the results are tabulated in table 2.

In both parts of the study a total of five patients complained of irritation and increased pruritus caused by both the prednisolone and hydrocortisone creams, although only three of these showed objective clinical evidence of an allergic eczematous reaction in the areas where the medicaments were applied. These five patients were given patch tests with the water-washable base, with prednisolone alcohol (0.5%) in a petrolatum base, and with hydrocortisone free alcohol (1%) in a petrolatum base, the medicaments having been applied under a standard closed patch and read after 48 hours. The three patients who had an eczematous reaction clinically showed a positive reaction to the water-washable base only. None of the five patients tested showed a positive reaction to either the prednisolone or hydrocortisone in the petrolatum base. In the other two patients, patch tests were negative, and further patch tests to both the prednisolone and hydrocortisone creams were likewise negative. Two other patients complained of slight irritation from the hydrocortisone cream, despite a definite objective improvement of the lesions. Thus, seven patients complained that one or both of the medicaments caused some degree of irritation subjectively. Only three of these proved to have an actual allergic eczematous reaction, and this was to the water-washable base itself. There was no single instance of an allergic sensitization to either the prednisolone alcohol or the hydrocortisone free alcohol.

TABLE 1.—*Comparison of Prednisolone Alcohol (0.5%) Cream with Hydrocortisone Free Alcohol (1%) Cream*

Dermatoses	Total No. of Cases	Prednisolone More Effective	Prednisolone Equally Effective	Prednisolone Equally Ineffective	Prednisolone Less Effective	No Comparison
Allergic contact dermatitis	43	20	14	6	2	1
Seborrheic dermatitis	27	8	14	2	3	0
Atopic dermatitis	23	9	9	0	4	1
Pruritus ani (or vulvae)	12	1	2	2	1	6
Lichen simplex chronicus	9	4	2	1	1	1
Nummular eczema	4	1	1	2	0	0
Stasis dermatitis	3	0	0	3	0	0
Urticaria, acute	3	1	2	0	0	0
Dermatitis herpetiformis	2	0	2	0	0	0
Dermatophytid reaction	3	1	2	0	0	0
Otitis externa	3	1	2	0	0	0
Prurigo mitis	1	0	0	1	0	0
Miliaria rubra	1	1	0	0	0	0
Erythema multiforme bullosum	1	1	0	0	0	0
Dermatitis medicamentosa	1	0	1	0	0	0
Discoid lupus erythematosus	1	0	0	1	0	0
Total	137	48	51	18	11	9

TABLE 2.—*Comparison of Prednisolone Alcohol (0.5%) Cream with Placebo Water-Washable Base (Procutan)*

Dermatoses	Prednisolone More Effective	Prednisolone Equally Effective	Prednisolone Equally as In-Effective	Prednisolone Less Effective	Total No. of Cases
Allergic contact dermatitis	5	1	0	1	7
Atopic dermatitis	5	0	0	0	5
Seborrheic dermatitis	3	0	1	0	4
Pruritus ani	2	0	0	0	2
Nummular eczema	1	0	1	0	2
Lichen planus	0	0	1	0	1
Pruritus hiemalis	1	0	0	0	1
Lichen simplex chronicus	1	0	0	0	1
Pemphigus vulgaris	1	0	0	0	1
Total	19	1	3	1	24

Although no determinations of serum sodium level were done, there was no instance of ankle or leg edema indicating possible systemic absorption of either the prednisolone or hydrocortisone free alcohol, even when the medicaments were applied over extensive areas of the body.

Summary and Conclusions

The clinical effectiveness of topically applied prednisolone alcohol was evaluated by the simultaneous paired comparison method in 137 patients with various selected dermatoses. Of a total of 128 patients in whom the clinical effect of prednisolone alcohol (0.5%) in water-washable base was compared with that of hydrocortisone free alcohol (1%) in the same base, the prednisolone alcohol proved to be more effective in 48 cases, the two were equally effective in 51 cases and equally ineffective in 18 cases, and the hydrocortisone free alcohol was more effective in 11 cases. Thus, in 99 out of 128 cases (77%) the prednisolone alcohol was more effective than, or equally effective as, the hydrocortisone free alcohol, although it was used in one-half the concentration of the latter. In 24 cases in which the clinical effect of prednisolone alcohol (0.5%) in water-washable base was compared with that of the empty water-washable base, the prednisolone was much more effective in 19 cases, the two were equally effective in one case and equally ineffective in 3 cases, and the prednisolone was less effective than the water-washable base in only one case. Of a total of five patients who complained of irritation from either the prednisolone alcohol or the hydrocortisone free alcohol creams, three showed allergic eczematous reactions to the empty water-washable base when applied in a closed patch test. There was no instance of an allergic sensitization to either the prednisolone alcohol or the hydrocortisone free alcohol. No evidence of undesirable side-effects from systemic absorption of the medicaments was noted.

These results indicate that prednisolone alcohol, when used in only one-half the concentration of the hydrocortisone free alcohol, is as effective as, or slightly more effective than, hydrocortisone free alcohol in the topical therapy of various dermatoses such as allergic contact dermatitis, atopic dermatitis, and pruritus ani. It would appear then that, upon topical application, prednisolone alcohol is approximately twice as effective, milligram for milligram, as hydrocortisone free alcohol. It should prove to be a most useful addition to the dermatological armamentarium.

454 New York Ave.

The prednisolone alcohol (0.5%) cream and hydrocortisone free alcohol (1%) cream used in this study were supplied as Meti-Derm and Cortifan, respectively, by the Schering Corporation, Bloomfield, N. J.

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UNITIZED DISPOSABLE URETHRAL CATHETER AND SPECIMEN CONTAINER

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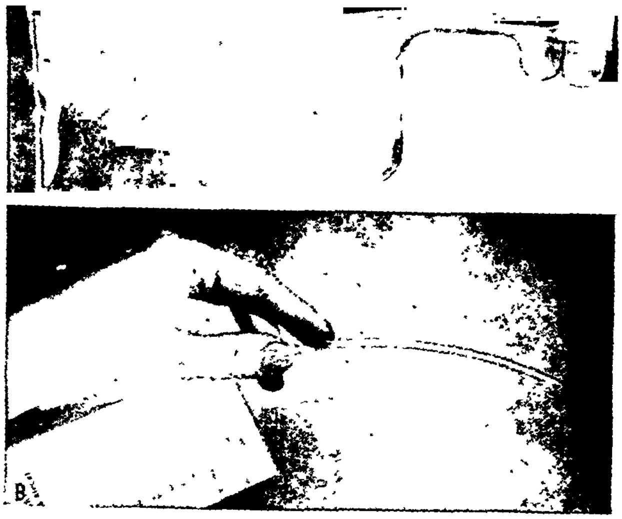
and
Donald W. Smith, M.D., Miami, Fla.

Significant laboratory examination of urine from the female requires that the specimen be collected by catheter in a clean container. Urine voided directly into a bottle or bedpan often contains foreign material, including epithelial cells, mucus, pus or blood from adjacent perineal areas, or extraneous substances from the collection container. While a negative voided specimen is significant, a positive one requires restudy of a catheterized specimen in order to determine the significance of the findings. Such duplication is time-consuming and, therefore, costly.

The method of catheterization of the bladder in the female most commonly used involves the use of a sterile rubber catheter to protect the patient from extraneous contamination, a rubber glove to handle the sterile catheter, and a suitable collection container. Each of these items must be reprocessed before each use. Since this takes time and is, from the labor standpoint, costly, and because the equipment tends to deteriorate rapidly, catheterization is sometimes neglected when it should be accomplished. This problem has stimulated us to originate a piece of equipment that will serve at a maximum saving of both time and money.

The device consists of a plastic catheter enclosed in a flexible plastic specimen container, which is sealed and sterile (see A in figure). An identification card is attached. Both unit parts are made of polyethylene because of its inert nature, relative freedom from foreign material, and smooth surface, combined with optimal stiffness and strength. After one use, both



Unitized disposable urethral catheter and specimen container, *A*, before container is opened, and *B*, ready for use.

From the Department of Surgery, Jackson Memorial Hospital.

the catheter and container may be discarded, eliminating the problems of washing, sterilization, and other intermediate handling. The catheter is suitably tipped and cut on the side to provide for adequate flow of urine without risk of traumatizing urethral surfaces during the insertion. The thin catheter wall provided by the plastic permits an outside diameter equal to that of a 12 F. catheter and a lumen equivalent to that of a 15 F. rubber catheter. This large internal diameter permits a more rapid flow of urine, useful in both specimen collection and emptying the bladder for pelvic examination. The back end of the catheter is flared making it easy to handle and express from the bag and also permitting the attachment of a syringe for bladder irrigation and aspiration.

An arm of the bag holds the tip of the catheter in place and ready for use. The bag is opened at the end containing the catheter tip by tearing a tab off, and the catheter is expressed as seen in *B* in the figure.

As the flared end of the catheter is slightly larger than the neck of the bag, the bag will not fall off. It is not necessary to wear a sterile glove to handle the catheter since it may be held by the portion remaining in the specimen container. The external meatus is prepared, the catheter inserted, and the collection bag filled. If it is desired to empty the bladder, the bag is pulled from the catheter and the remaining urine is collected in a basin. The bag is sealed by folding over the neck and fixing it to the card with the attached clip. The card has space for pertinent information identifying the patient and doctor and regarding the studies desired. It goes with the bag to the laboratory where other spaces are filled in with the results of the examination, and the entire card is returned to the physician.

We believe that a unitized sterile catheter and specimen container, of the nature described, will greatly facilitate the success of studies of urine in the female by making every specimen study a significant one and by eliminating the time and cost of equipment preparation.

25 S. E. Second Ave. (Dr. Smith).

This unitized disposable urethral catheter and specimen container is manufactured by Dade Reagents, Inc., Miami, Fla., and may be obtained under the name "Cath-Urine" from surgical supply houses.

COUNCIL ON PHARMACY AND CHEMISTRY

REPORT TO THE COUNCIL

The Council has authorized publication of the following report. Nonproprietary terminology is used for drugs that are mentioned; when such terminology is not considered to be generally well known, its initial appearance is supplemented by parenthetic insertion of names known to be applied to commercial preparations. H. D. Kautz, M.D., *Secretary.*

CURRENT STATUS OF THERAPY IN HYPERTENSION

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and
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Means for controlling the excessive generalized vasospasm found in patients with chronic arterial hypertension have greatly improved during the past 5 years. The development of new drugs with specific actions has pointed up the several mechanisms that act together to cause vasospasm; it has resulted in alterations toward or to normal of a disturbed physiological and biochemical state and has effected considerable reduction in morbidity and mortality and sometimes remarkable clinical improvement in patients suffering from fatal forms of the disease. Furthermore, the question of what is cause and what is effect has been clarified. The results in well-treated patients, formerly suffering from hypertension of severe degrees and often with serious secondary conditions, may be summarized as follows: a virtual disappearance of congestive heart failure, formerly the major cause of death; considerable reduction in incidence of cerebral vascular accidents, especially hemorrhage; slowing, halting, or even regression of progressive renal functional damage; and halving of the 100% mortality (for at least three years) in cases of malignant hypertension that have advanced to azotemia. In a sizable proportion of cases, the underlying process has apparently reversed itself enough to allow drastic reduction of doses or even discontinuation of therapy. Thus neurosurgery has become unnecessary except in selected cases, and other less specific forms of therapy have been made obsolete.

In order to understand the rationale for the use of the several drugs and methods, a brief résumé of present concepts of basic pathogenesis is in order. Intermittent, rapidly fluctuating generalized vasospasm is considered to be neurogenic, mediated through the sympathetic portion of the autonomic nervous system or, in the unusual case of a pheochromocytoma, by the sympathetic effector substances, levarterenol (norepinephrine) and epinephrine. Drugs are available that act upon sympathetic areas in the brain, upon autonomic ganglia, and, for diagnostic purposes, upon the sympathetic effector substances at the junction of nerve and vascular smooth muscle. Surgical sympathectomy accomplishes the same result to some degree.

Certain known and some unknown factors in time convert intermittent neurogenic vasospasm into chronic sustained vasospasm. This form is mediated by

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humoral, probably nephrogenic, vasoconstrictor substances. A different type of drug, acting directly upon vascular smooth muscle, is available to counteract this influence. The drug also has the capacity to destroy the activities of most known and suspected humoral pressor substances implicated in hypertension. When hypertension becomes chronic, therefore, both humoral (nephrogenic) and neurogenic influences operate together, the former engrafted upon the latter. Renal ischemia is the invariable accompaniment.

In certain cases of overt localized disease of the adrenal cortex (adenoma), and perhaps to a slight degree in many other cases of hypertension, vascular smooth muscle becomes sensitized both to normal and to abnormal vasoconstrictor influences, neurogenic and humoral. Sensitization is mediated through the sodium ion plus sodium-retaining steroid hormones. Overproduction of adrenal cortical salt-retaining hormones can probably affect intracellular constituents of electrolytes. In the ratio $Na^+ + K^+ + OH^-/Mg^{++} + Ca^{++} + H^+$ muscular irritability is increased by an increase in the numerator and decreased by an increase in the denominator. Because renal ischemia even of a slight degree is associated with urinary loss of sodium chloride, presumably the adrenal cortex is stimulated to produce more salt-retaining steroids than usual. Methods for counteracting this influence include adrenalectomy, metabolic antagonists to specific steroid hormones, and depletion of sodium from the body. This influence is usually of secondary pathogenetic importance except when functioning adenomas are present, when it can be primary. Thus it is obvious that when two vasospastic influences act together to cause hypertension, two counteracting drugs or methods must be used to achieve reversal of vasospasm.

Drugs and Procedures Available

Drugs Acting Directly or Indirectly on Central Sympathetic Areas.—Alkaloids from species of Rauwolfia, of which reserpine is one, act on cerebral centers. Reserpine, a very mild antihypertensive agent, acts by displacing serotonin from receptors in corticohypothalamic tracts, especially those to the posterior (sympathetic) portion of the hypothalamus. Although the drug is rapidly excreted, these receptors are blocked for several days. The result is a reduction of the sympathetic outflow and relative parasympathetic overactivity; therefore, nervous reactions to stress by vasospasm are partly inhibited. This drug also releases serotonin from platelets and the intestines. Its usual side-effects are many and frequent. Those resulting from parasympathetic overactivity are bradycardia, gastric hyperacidity, and gastrointestinal hypermotility (peptic ulcer has apparently been activated and ulcerative colitis initiated by reserpine). Those probably resulting from serotonin depletion are loss of affect, drive, ambition, and the ability to form new concepts and meet new situations (effects similar to those of a medical prefrontal lobotomy). Increased appetite and decreased nervous energy may lead to obesity, and nasal stuffiness has occasionally caused epistaxis in older individuals with atherosclerotic arteries. More serious late side-effects, possibly caused by excessive depletion of serotonin, are anxiety, nervousness, insomnia, and wild dreams and nightmares; eventually, agitated depressive psychosis with suicidal tendencies may occur, which places it among the drugs with occasional fatal reactions. Return of function after a psychosis has developed may be delayed for several weeks or months.

The dosage-response curve to reserpine is extremely flat; therefore, large initial doses (1 to 4 mg.) can be given safely. The mild hypotensive effect precludes any exact statement as to optimal dosage, although frequently a dose of 0.1 to 0.25 mg. is satisfactory for maintenance. Since some effect usually persists for weeks, a single daily oral dose is adequate. Normotension is usually achieved by this agent only in the mildest cases with considerable emotional overlay.

Chlorpromazine (Thorazine) is also a serotonin antagonist, although its primary action is not to paralyze cerebral serotonin receptors but rather to affect the vasomotor center in some manner. Large doses produce not only bradycardia and a slight to moderate fall of blood pressure but also many side-effects. Thus it is of little value as an antihypertensive agent other than indirectly through its sedative action.

Protoveratrines A and B (Veralba), two alkaloids extracted from species of Veratrum, act at a similar or lower level by stimulating the carotid sinus and aortic depressor nerves (the baroreceptors), thus causing an increase in their depressor activity. The pathway is through the glossopharyngeal nerve to the vasomotor center. Side-effects caused by vagal stimulation include bradycardia, increased gastrointestinal motility, gastric hyperacidity, nausea, and vomiting. Intermittent hypotension or normotension can be achieved only by careful regulation of dose, which varies from one individual to another.

The initial dose of protoveratrines A and B, most satisfactory when given orally, is 0.5 mg. three times a day. This dose is increased by increments until the desired effect is produced or nausea supervenes. Ordinarily the margin of safety between therapeutic and toxic doses is low, making dosage critical. The very rapid appearance of tolerance precludes the maintenance of normotension with this agent alone.

Drugs Acting to Interrupt Somatic Autonomic Nerves.—Of the four drugs most commonly used clinically to interrupt somatic autonomic nerves, one is a secondary amine and three contain tetracovalent nitrogen (quaternary ammonium) as does acetylcholine. Special configurations in the molecules apparently cause predilections for autonomic ganglia, just as other configurations of tetracovalent nitrogen promote acetylcholine inhibition at myelinated nerve endings on striated muscle (curare, succinylcholine, decamethonium, and other curariform drugs).

The four orally effective blocking agents are hexamethonium, pentolinium (Ansolysen), chlorisondamine (Ecolid), and mecamylamine (Inversine). The amine, mecamylamine, is entirely absorbed from the gastrointestinal tract, while the three quaternary ammonium drugs are absorbed to varying and unpredictable extents. All have similar clinical effects and durations of action. No evident metabolism has been shown for any of them, and all are excreted by the kidney. Potentiation of autonomic blockade results from gastrointestinal hypomotility, which allows increased absorption; renal failure, which delays excretion; and diminished intake of sodium. Tolerance is characteristic of blocking agents when they are used alone. Moreover, the danger of postural hypotension ordinarily precludes lowering the blood pressure to normal in any but the erect position, with the result that some authorities insist on the patient sleeping on an incline with the head up. Both tolerance and postural hypotension usually may be prevented by simultaneously administered hydralazine (Apresoline).

The pharmacological effect of autonomic blocking agents is that of both sympatholysis and parasympatholysis. The desired antihypertensive effect results from sympatholysis. Excessive hypotension may rarely lead to renal failure requiring levarterenol (Levophed) for its control. Undesired side-effects result from parasympatholysis; the major ones are retention of urine and intestinal paralysis. The minor ones include loss of visual accommodation, dryness of mucous membranes, and diminution of normal sweating.

The required dose of autonomic blocking agents is unpredictable and must be determined separately for each patient. The effect can often be enhanced and rendered more reproducible if these drugs are taken on an empty stomach. Orally mecamylamine is about 50 times as effective as hexamethonium, 10 times as effective as pentolinium, and 5 times as effective as chlorisondamine. For each the duration of action of a single dose varies between 3 and 6 hours, hexamethonium being the shortest acting and chlorisondamine and mecamylamine having the longest effect. The wide variety of advocated regimens reflects the differing goals of therapy as well as the variability of individual patients.

The autonomic blocking agents can be used parenterally in hypertensive emergencies such as encephalopathy and cardiac failure. Even when injected, the required dose is unpredictable. In general, the more acutely a patient requires therapy, the less drug he needs. The maximum safe initial dose of hexamethonium chloride, given subcutaneously or intramuscularly, may be as little as 0.25 mg. Larger doses can be given into an extremity when a tourniquet can be placed above the site of injection, or by slow intravenous drip, the blood pressure being "titrated" to the desired level. If circulation is adequate, doses given subcutaneously can safely be successively doubled at 10-minute intervals until sufficient lowering of the blood pressure is obtained. To maintain normotension, as much as 25 or 50 mg. of hexamethonium given subcutaneously may be needed every 4 hours. When necessary the systolic pressure can often be maintained within a range of 20 mm. Hg by parenterally given autonomic blocking agents. In our experience, this can best be done by giving a full dose every 1, 2, or 4 hours if the systolic pressure is above the desired range, half the dose if it is within the range, and none if it is below the range. The mean pressure can then be lowered on successive days depending on the patient's condition. In those rare cases in which gastrointestinal symptoms require substitution of long-continued parenteral therapy, the average maintenance dose of intramuscular hexamethonium approximates one-twentieth of that required by mouth. For pentolinium the parenteral dose approximates one-fifth of the oral dose; for chlorisondamine, two-fifths; and for mecamylamine, the two are equal.

When localized atherosclerosis is present, the violent fluctuations of blood pressure sometimes induced by drugs can be hazardous. Ischemia may result either from a lowered blood pressure in vessels that cannot dilate as widely as the remainder of the vascular system or from thrombosis beginning on an atherosclerotic plaque when blood flow is impaired. Thus, cerebral thrombosis, mesenteric thrombosis, and coronary thrombosis have occurred rarely and must be kept in mind when atherosclerotic patients are treated. Ischemia has also caused depression, temporary loss of memory, worsening of anginal pain (rare), and temporary diminution of renal function (not to the extent of azotemia, however).

In the small and very seriously ill group of patients with true malignant hypertension that has progressed to the point of azotemia, hexamethonium has produced a fatal pulmonary disease characterized by fibrinous pneumonitis. Hexamethonium is the only autonomic blocking agent associated with this type of toxicity; moreover, the entity has become rare in the last 2 or 3 years, perhaps because other ganglionic blocking agents are more popular and control of hypertension is better achieved. Poor and intermittent control of hypertension has usually preceded pulmonary symptoms. Tachypnea, becoming worse in the sitting or standing position, is a cardinal sign. The microscopic lesions resemble those of "uremic pneumonia" despite the presence of only moderate azotemia (no more than 60 mg. of nonprotein nitrogen per 100 ml. of plasma) and the absence of clinical uremia. One patient may have recovered after treatment with cortisone.

In this same small group of very seriously ill patients with true malignant hypertension that has progressed to the point of azotemia, large doses of mecamylamine have produced a nonfatal, reversible disturbance characterized by generalized and severe coarse or flapping tremor that disappeared with sleep. Intense anxiety, sometimes with hallucinations, has also occurred. The syndrome resembles delirium tremens rather than Parkinsonism. Recovery has taken as long as 1 to 2 weeks after withdrawal of the drug and substitution of another agent.

Drugs Acting Directly on Vascular Smooth Muscle.—Hydralazine relaxes constricted vascular smooth muscle. Notable among its effects is an increase in renal plasma flow, reversing the hemodynamic profile accompanying hypertension. It is unique in that this action is duplicated only by pyrogens and pregnancy. Another important effect includes inactivation of pherentasin, the vasopressor polypeptide found in human hypertensive blood, and inactivation of hypertensin or angiotonin, the vasopressor polypeptide resulting from the proteolysis of a plasma globulin by renin from the kidney. It is likely that pherentasin is activated human angiotonin. In vitro, hydralazine inhibits at least one decarboxylase, that of dihydroxyphenylalanine, and stimulates monamine oxidase, the ubiquitous enzyme that can deaminate many substances with vascular and cerebral actions such as hypertensin, pherentasin, serotonin, levarterenol, epinephrine, tyramine, and tryptamine. Some of these are the products of amino acid decarboxylation. Hydralazine is also a strong chelating agent for some trace metals. In these respects its actions on the humoral nephrogenic mechanisms of hypertension are ideal, as it causes vasodilatation, increased renal blood flow, and both diminished production and increased destruction of vasoactive substances found or suspected in blood. Hydralazine should therefore be a basic medicament in all forms of the disease in which a nephrogenic, humoral influence is present. It must be given in large doses to patients in whom this influence is great.

There are unwanted and undesirable actions of the drug. Histaminase is inhibited in vitro; some of the symptoms that appear when hydralazine is given, including headache, flushing, aching, edema of the skin, and nasal stuffiness, may be attributed to failure of destruction of histamine. Mild chemosis is common; tachycardia is produced, but it may be inhibited by drugs given adjunctively that act on the nerves. Occasionally drug sensitivity with fever, aching, and flulike symptoms appears. In a few individuals the drug cannot be used at all.

Late toxic reactions generally are confined to a syndrome simulating disseminated lupus erythematosus, characterized usually by arthritis or arthralgia in the early stages, with malaise, lassitude, and weakness. Splenomegaly, hepatomegaly, and lymphadenopathy are sometimes seen; evidence of disturbance of circulating protein levels is almost always found, with increased cephalin cholesterol flocculation and thymol turbidity of serum and hyperglobulinemia. Leukopenia and anemia have been seen and the L. E.-cell preparation of blood eventually becomes positive. If administration of the drug is discontinued, these symptoms and findings regress and disappear; if not, symptoms may subside only to recur. The main organic change is progressive renal dysfunction with azotemia, which does not, in our experience, regress or progress after the drug has been omitted. This syndrome has been reproduced in dogs, with the appearance of "wire-loop" lesions of glomeruli. "Hydralazine disease," which occurs in 8 to 10% of individuals, is rarely seen in patients taking 0.4 gm. a day or less. It develops in 5 months to 4 years, cannot be made to develop deliberately by very high doses, and is completely, if slowly, reversible when administration is discontinued. The phenomenon resembles a syndrome of depletion in many respects and one of hypersensitivity in others. By reducing the dosage slowly and carefully after 6 months of therapy to 0.4 gm. a day or less, this high rate of reaction can be lowered. By no means does it negate the use of this valuable drug. Furthermore, it stimulates research and development of analogous substances, among which are many experimental compounds that chelate or bind trace metals. Thiocyanate, nitroprusside, azides, and dimercaprol (BAL) have been used in man; many other binding agents have been tried in hypertensive animals. Other compounds that act on constricted vascular smooth muscle and destroy hypertensin and pherentasin but are less toxic are sorely needed.

Agents and Methods Affecting Vascular Smooth Muscle by Interfering with Salt-Steroid Relationships.—No drugs are available as yet that will compete with aldosterone (11β-21-dihydroxy-3,20-diketo-4-pregnene-18-al) or other salt-retaining hormones and therefore depress the reactivity of vascular smooth muscle; however, experimental agents that will do this have been synthesized. Until specific antialdosterones are found, the only recourse is dietary restriction of sodium. The restriction must be strict and considerable, to 0.5 gm. of salt per day, a regimen difficult to achieve for the average patient.

The physician should understand what he is doing when salt is restricted. The kidney of a patient with hypertension, even in the mildest stages, loses salt. The effect of salt restriction is to cause overactivity of the zona glomerulosa of the adrenal cortex. The expected result is excessive production of aldosterone, just as this hormone is produced in salt-retention states such as edema. Because salt-retaining hormones plus sodium ion apparently sensitize vascular smooth muscle to vasoconstrictor substances and impulses, removal of either may negate excessive sensitivity, but removal of sodium may cause overproduction of the other. Too severe salt depletion will lead to the low-salt syndrome, with renal insufficiency and death. Thus salt restriction of a degree sufficient to lessen vascular reactivity must be carefully achieved in order to avoid both insufficient and excessive loss of sodium. The relatively few fatal reactions observed indicate that the error is largely on the side of insufficient depletion.

Methods of Administration

The use of potent hypotensive agents cannot be haphazard, intermittent, or careless. There is no better method for producing intractable tolerance to their actions in severe hypertension than by discontinuous, uneven therapeutic pressure. Once started, they must be given at regular intervals, in doses adequate to produce the desired effects. Side-effects are treated as they arise; with ganglionic blocking agents they are averted before they appear by the use of laxatives and parasympathomimetic drugs.

The aim of therapy is to cause mean diastolic normotension or, failing that, a reasonable facsimile thereof. Compromises with normotension result in compromises with the disease. The upper limit of diastolic normotension is defined as 90 mm. Hg. To achieve it requires education of the patient, a physician familiar with the pharmacological actions of various drugs, duration of action and side-effects, and careful instruction in self-medication. It also requires data on levels of blood pressure, secondary effects of the disease, and progress of the patient. Failing that, control is erratic and hazardous. No attempt is made to achieve systolic normotension (140 mm. Hg) in patients with severely atherosclerotic aortas.

The *sine qua non* of effective therapy of chronic generalized vasospasm is to use one agent acting on neurogenic vasoconstrictor mechanisms and one agent acting on vascular smooth muscle. No single drug combines these two actions.

Milder forms of the disease respond to milder measures, more severe forms to more potent drugs and vigorous measures. Unfortunately, the durations of action of all of the orally effective available ganglionic blocking agents are short, 4 to 6 hours, and they must be given at these intervals. When one of the hypertensive mechanisms, either the neurogenic or nephrogenic, is blocked, the other appears to "overshoot" or become hyperactive. Thus, in severe cases, and even in less severe ones, both types of agents are essential for control.

In milder cases, when hypertension is present upon examination by a physician and during emotional stress but is probably absent during sleep and relaxation, reserpine alone, 0.1 to 0.5 mg. given orally per day, may be tried for a month or two. If this is not effective, hydralazine hydrochloride is added in doses of 25 mg. four times a day, increasing at weekly intervals until 300 or 400 mg. per day is given. The maximal effect can be observed in one to three months. This method is justifiable only when the physician is relatively certain that a cardiovascular accident will not occur in that interval or that renal deterioration is not present and progressive. A false sense of security may be engendered by the very fact of treatment, even though treatment is inadequate or useless.

In more severe cases, those in which hypertension does not respond completely to sedation, relaxation, bed-rest, or sleep induced by amobarbital (Amytal) sodium, or in patients with persistent hypertension leading to cardiovascular accidents, ganglionic blockade and hydralazine are indicated. Ganglionic blockade is initiated more safely and easily in the hospital.

Blood pressure is measured by competent nurses every 4 hours, day and night, and charted. The choice of a ganglionic blocking agent is a matter of individual preference. Hexamethonium chloride (125 mg.), pentolinium tartrate (20 mg.), chlorisondamine chloride (12.5 mg.), or mecamylamine hydrochloride (2.5 mg.) are given orally every 4 hours around the clock. In order to avoid undue intermittent hypotension, doses are omitted if the systolic pressure is below a chosen level, usually 140 mm. Hg for younger individuals and 150 or 160 mm. Hg for those with atherosclerosis of the aorta, cerebral thrombosis, or ischemic manifestations caused by local atherosclerosis. Some physicians take the blood pressure with the patient supine, whereas others take advantage of postural effects and measure it with the patient seated. Measurement with the patient in the standing position should be avoided, for falsely low values and insufficient doses will result. Laxatives should be given as needed to prevent constipation and the consequent danger of paralytic ileus in patients receiving ganglionic blocking agents by mouth.

The dose of ganglionic blocking agent is raised every day by increments similar to the initial dose until fluctuations to normotensive pressures occur. In the usual case of moderately severe hypertension, 500 mg. of hexamethonium chloride, 100 mg. of pentolinium tartrate, 50 mg. of chlorisondamine chloride, or 10 mg. of mecamylamine hydrochloride every 4 hours is sufficient to produce this effect, although twice these doses occasionally becomes necessary. Rarely is normotension (mean pressure, 140/90 mm. Hg or below) achieved and maintained by these drugs when used alone, partly because of irregular absorption, rapid elimination, and increasing tolerance.

If protoveratrines A and B are preferable, an initial dose of 0.5 mg. is given three or four times daily during the day and increased daily by 0.5 mg. at first and then by 0.2 mg. until nausea or vomiting occur. The dose is then reduced by 0.2 mg. Patients vary considerably in their reactions to this agent; since there is some carry-over from one dose to another during the day, the morning dose will be relatively high (2 mg. or more), the noon dose less (1 mg.), and the evening dose greater or less. The production of fluctuations to normotensive levels at doses less than those causing nausea is the aim; each dose is critical in this respect.

At this point 25 mg. of hydralazine hydrochloride is administered every 4 hours. At daily intervals this dose is successively doubled, tripled, and finally quadrupled. If normotension is not achieved, the dose of blocking agent or hydralazine is increased, depending upon clinical judgment and findings as to whether neurogenic or nephrogenic influences are greater. In unusual cases of sensitivity, this drug cannot be used. During the appearance of sustained normotension or considerable fall in blood pressure, the patient often complains of weakness, lethargy, lassitude, prostration, and poor memory. He then needs encouragement, for these symptoms pass in a few days or weeks.

Before the patient leaves the hospital, the night dose is omitted and blood pressure is measured always with the patient sitting. Doses of blocking agents automatically adjust themselves downward by this procedure, although higher levels are usually found in the morning because the agent is excreted during the night. The patient is taught to take and record his own pressure and is discharged from the hospital to continue on five doses of blocking agent and hydralazine per day, the former on a sliding scale depending upon prevailing levels of systolic pressure. The effective dosage of ganglionic blocking agents is usually less during warm weather. The rationale and limits of therapy are carefully explained. In our experience, only rarely is a patient made nervous or neurotic by self-medication and self-measurement; on the contrary, a sense of relief and freedom from anxiety is provided him by learning that he can lower his blood pressure by a tablet.

If data are adequate (frequent readings of blood pressure) and suggest a reduced drug requirement, after 6 months of therapy in some cases and after a year in others, the doses may be decreased to four times a day. A rise in the mean pressure level during the next week or two requires readjustment of the dose upward. After 2 or 3 years, especially when little ganglionic blocking agent is needed, the amount of hydralazine hydrochloride may be lowered slowly to very small quantities, 25 mg. per day, or even omitted. If, however, diastolic normotension is not achieved, no reduction in dosages is advisable.

Withdrawal of both drugs, unless by gradual decrements as described, results in a return of hypertension. If the patient formerly exhibited the malignant stage (hemorrhagic and exudative retinitis, papilledema, high fixed diastolic pressure, and renal damage), that stage may return abruptly in a day or two, with subsequent deterioration and death resulting from a cerebral vascular accident or an episode of congestive heart failure. If a patient is once committed to therapy, therefore, he should continue until it no longer becomes necessary. Whether or when that time will arrive cannot be foretold.

There are alternate choices of combinations of these drugs and methods, suitable for individual cases. Ordinarily, none of these drugs will give an optimal result when used alone; however, a drug or measure acting on autonomic nerves can be combined with one acting on vascular smooth muscle with additive results. Thus, reserpine, surgical sympathectomy, or ganglionic blockade can be satisfactorily added either to dietary restriction of salt or to hydralazine. In our experience, the combination of two measures in the first group provides erratic control, while the combination of two in the second is little more effective than either one alone.

The potencies of the different drugs and combinations of drugs in counteracting generalized vasospasm can be expressed briefly as follows from mildest to strongest: reserpine, reserpine plus hydralazine, protoveratrines A and B, chemical ganglionic blockade, protoveratrines A and B plus hydralazine, and ganglionic blockade plus hydralazine. If a strict low-sodium diet (0.5 gm. of sodium chloride per day) can be attained, its effect can be considered approximately equal to that of hydralazine alone; therefore, it may be substituted for hydralazine in any one of the previously mentioned combinations. Hydralazine alone is seldom given unless surgical sympathectomy has been performed.

From the foregoing data, it is obvious that the use of a single capsule or tablet containing a combination of two or more potent agents is unduly restricting and may even be hazardous. Each type of drug acts upon a different area, and the dose must be adjusted to suit the individual. Regarding side-effects of ganglionic blockade, this is one of the rare examples in which one is justified in setting one pharmacological thief to catch another; however, a blocking agent combined with a standard dose of neostigmine (Prostigmin) or bethanechol (Urecholine), for example, given in varying doses, might be expected to cause unpredictable results. These combinations of two oppositely acting drugs are avoided. Furthermore, there is no more justification for giving reserpine, a drug with prolonged action, in slowly released doses from a capsule, than there is in giving digitalis in such a preparation. Each agent is given for its specific action in the dose that will produce the desired effect without undue toxic effect.

Summary

Modern drugs and methods provide a relatively safe and effective, though difficult, form of therapy for combating the excessive vasospasm to which arterial hypertension is secondary. Undesirable side-effects are common to all. If the drugs are to be used to their best advantage, a physician familiar with their primary actions and side-actions and a patient educated in their use are essential. Prolongation of life, lessening of cardiovascular-renal accidents and deterioration, and regression of the basic disease have been demonstrated. No patient need live with hypertension if he is willing to endure the inconveniences of therapy.

This study was supported by a grant-in-aid from the National Heart Institute, U. S. Public Health Service, and the Lasdon Foundation.

COUNCIL ON INDUSTRIAL HEALTH

The following Committee Report was approved for publication by the Council on Industrial Health on Oct. 27, 1956. B. Dixon Holland, M.D., *Secretary.*

THE SURVEY OF THE OCCUPATIONAL ENVIRONMENT

AN ESSENTIAL OF INDUSTRIAL MEDICAL PRACTICE

Introduction

This treatise is intended primarily for those physicians who serve industry on call; those physicians whose private clientele includes industrial employees; and those to whom industrial employees come for preplacement, periodic, or other types of physical examination, diagnosis, or treatment. Its purpose is to promote greater interest, knowledge, and activity in occupational health on the part of all physicians who are, or should be, concerned. Full-time industrial medical directors and staff physicians presumably are well acquainted with the matters discussed, as are most physicians occupying such positions part time. However, they might find in this treatise worthwhile reminders.

The physician may gain much through a personal survey of the occupational environment of persons who are under his supervision or of those who are or may become his patients. Increasingly in the large plant and especially where there is a well-organized medical department, the industrial physician observes operations and the conditions under which the employees are working. This practice should be adopted by the physician who has an "on-call" relationship with industrial plants. After each survey, the physician should discuss his observations with management with particular recognition of the fact that the assistance of several disciplines is usually necessary to control a given situation.

General practitioners whose patients include industrial workers can and should acquire some knowledge of the industrial operations of the area through organized plant tours or invitational open-house arrangements between the industries and the local medical society.

Manifold advantages are to be gained from a survey of the occupational environment. The information obtained may permit the physician more adequately to diagnose and treat disease affecting his patient. As an example, a persistent hepatitis may fail to respond to treatment. Inquiry into the patient's occupation may disclose exposure to a chlorinated hydrocarbon solvent vapor as the possible cause. Only after this exposure is evaluated and brought under satisfactory control

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This report was prepared by the subcommittee to revise "Plant Hygiene Studies" of the Committee on Interprofessional Relations, Council on Industrial Health, American Medical Association. The following persons are the members of the subcommittee: Warren A. Cook, Chairman, William G. Hazard, Herbert T. Walworth, Irving R. Tabershaw, M.D., and Jerome K. Brasch.

can the patient's hepatitis be alleviated and, of equal importance, development of hepatitis in other workers at the operation be avoided.

Similarly, the survey permits the physician to become familiar with the physical and mental demands of the job. It gives him the opportunity to see the people at work, in circumstances in which they are much more likely to be at ease than in his office. In addition he can become acquainted with materials and operations, the nature of exposure to substances and conditions that may affect health, and the physical conditions that may be the cause of accidents. It is important, however, at this point to caution the physician against hasty and unsubstantiated conclusions.

The physician is thus in better position to help in matching the physical abilities of a prospective employee with job requirements. He has a better understanding of the industrial health hazards as they actually exist in a given plant and at a specific operation. This knowledge of the environment permits him to take a more effective part in the prevention of occupational diseases and in accident prevention. What then is the first approach in making an initial survey of a plant and what should be looked for?

Preliminary to the Survey

Arrangements for an initial plant survey should be made invariably with management or an appropriate representative of management. Where the plant is small, there should be a discussion of the purposes of the survey with the head of the concern and the physician serving the plant. If the plant is a division of a larger organization, inquiry should be made through local management as to whether there is a medical director or consultant who supervises occupational health throughout all plants. If so, the physician should communicate with him. Both management and medical advisors would be expected to welcome such interest in plant conditions on the part of a general practitioner or on-call physician. In preparation for the survey, the physician should acquaint himself with the workmen's compensation act and the industrial health and safety regulations of the state.

In the actual conduct of the survey, management should designate someone familiar with the plant to accompany the physician through the various departments. In the larger concerns the safety director or the industrial hygienist would be the logical selection, since he would be well informed as to operations and potentially hazardous conditions, and as to the means of safeguarding workers against them. Prior to making the trip through the plant, the physician should discuss conditions with the person who is to accompany him.

A review of plant dispensary records should be made with special reference to minor complaints and injuries as well as lost-time injuries. It is to be hoped that there may have been some analysis of these data relative to major causes of injury, preferably in accordance with the code of the American Standards Association.[1] Special note should be taken of symptoms or complaints reported, particularly if recurrent in the same person or in different persons in the same department. If periodic physical examinations have been made, positive findings that may be associated with occupation help to point out those operations especially to be noted in the survey.

The Survey

Several types of surveys that vary in their purposes and thoroughness are well discussed by Patty.[2] He not only notes the information that should be gained in these surveys but also includes pertinent comments on proper conduct within the plant on the part of the person making the survey.

Conditions to be watched for are described briefly in the following paragraphs. Where such conditions are found, the physician should become more completely informed through references such as are listed by the Council on Industrial Health of the American Medical Association.[3]

POTENTIAL HEALTH HAZARDS

Injurious Materials

Dusts (Pneumoconiosis).—The hazard presented by dust in an occupational environment is dependent on a number of factors. It is necessary first to know something of its composition. Abrasive blasting may involve free silica in the form of quartz if a flint or sand abrasive is used. In this case, the dust exposure of the worker must be kept at a low level if silicosis is to be avoided. On the other hand, where steel abrasive is used to remove scale from steel forgings, the dust contains no silica and consequently need not be kept under as meticulous control as in the former instance.

The maximum amount of dust that can be considered acceptable depends not only on its composition but also on its particle size and the duration of exposure. Generally, dusts present in work atmospheres include appreciable proportions sufficiently small to reach the alveoli. The exceptions are rare. In regard to duration of exposure (not only to dusts but to other hazardous materials), an operation may be observed to be brief, but inquiry should be made as to whether it is repeated during the day, and how often. Where production involves a number of diverse operations, it is well to inquire whether activity at other periods during the day or week may involve exposures greater than those observed.

The dusts most likely to produce disabling pulmonary involvement are those containing free silica, that is, silicon dioxide not chemically combined with other elements. Such dusts occur frequently in industry. Inquiry should be specific in regard to this component, especially since the presence of free silica may not be readily apparent. For example, soapstone powder, widely used to keep layers of unvulcanized rubber from sticking together, may contain from 0 to 17% of free silica, depending on its source. The most common form of free silica is quartz, which occurs widely in nature. Natural materials widely used in industry that should be regarded as potentially productive of silicosis because of their high free-silica content are granite, flint, sandstone, sand, tripoli, and diatomaceous earth.

Dusts containing asbestos should also be noted, because prolonged exposure to asbestos dust in excessive concentration may result in a type of pneumoconiosis known as absestosis, which may be disabling. In coal mining and handling, attention should be given to the possible development of coal workers' pneumoconiosis, a recently recognized but incompletely explored clinical condition due to exposure to coal dust, per se, as well as to the possibility of silicosis from exposure to free silica in the rock associated with the coal in certain areas.

Metals and Their Compounds.—A large number of metals and their compounds are used throughout industry. As a potential industrial health hazard, the most prominent of these is lead, which may be present alone or in a wide variety of compounds. The chief mode of entry is inhalation of dust or fume. Percutaneous absorption of metallic lead and inorganic lead compounds is insignificant, but tetraethly lead and a few other organic compounds of lead may be absorbed through the skin under suitable conditions. Molten lead ordinarily does not present a hazard unless its temperature is well above its melting point. Special attention should be given to operations where lead may be subjected to temperatures above its boiling point, as in the welding of leaded steel. It is wise to have persons who work regularly with lead checked periodically for the extent of their lead absorption by determination of lead in blood or urine.

Lead compounds may be known by a number of names not including the word lead. Litharge, the common name for one of the oxides of lead, is found in the paste of lead storage battery plates, in a cement for attaching glass to metal, in "doctor" solution in petroleum refining, and in the manufacture of chrome yellow pigment. Although the specific gravity of this compound is high, litharge is often so fine that when dispersed into the atmosphere it will persist long enough to cause excessive exposure if adequate control measures are not in effect. In most industrial operations where dusty lead compounds are used or produced, it is desirable to have an evaluation of the exposure made with the aid of laboratory analysis of the air or of samples of the blood or urine of exposed employees, or by the combined investigation of the environment and the personnel.

Other toxic metals to which the physician should be particularly alert include antimony, arsenic, beryllium, cadmium, cobalt, manganese, mercury, and phosphorus. Exposure may occur in mining, metal-refining, fabrication, and metal-cleaning operations. Welding or high-temperature cutting on cadmium-plated surfaces can be particularly hazardous. The toxicity of beryllium is so extreme that it is in a category of its own. Mercury is of special importance because hazardous concentrations of vapor are released from the liquid metal even at room temperature. The dust of various mercury compounds is also toxic. Chromium in the form of chromic acid mist is commonly found in chromium electroplating or as salts of chromic acid in the form of dust, and may cause ulceration of the skin or the nasal septum. Zinc in the form of fresh zinc oxide fume, such as may arise from a bath of molten zinc at a galvanizing operation, may cause the temporarily disabling illness known as metal fume fever.

Excessive exposure to iron dust or fume as produced in welding, gas cutting, or grinding may cause sufficient retention in the lung to show as nodulation on chest films, but the condition is not regarded as disabling. These changes are somewhat erroneously interpreted as silicosis.

Whereas the pneumoconiosis-producing dusts usually require prolonged periods of exposure (years) to produce their effects, very brief exposures to toxic metals, solvent vapors, and gases can cause illness. Thus it is important that the physician be alert to the possibility that operations of brief duration may entail exposures more severe than those observed at the time of his survey.

Solvents.—In observing operations involving solvents, the physician should consider the possibility of absorption through the skin, in addition to absorption through the respiratory tract. Contact of these materials with the skin not only provides an avenue of introduction into the body but also presents the possibility of dermatitis.

There is a wide range of hazard potential among the many solvents used in industry. This is governed by the volatility of the solvent as well as by its toxicity. The exact chemical name of the solvent should be obtained. This need is illustrated by the two solvents, tetrachloroethylene and tetrachloroethane. There is only a slight difference in their names, but the toxicity of the former is indicated by a maximum acceptable concentration in the atmosphere of 200 parts per million as against 5 ppm for the latter—and they are of essentially the same volatility.

One of the frequent uses of solvents in a great variety of plants is in equipment known as the vapor degreaser. This is essentially a tank in which a solvent, often trichloroethylene, is vaporized by heating, and metal parts to be degreased are placed in the hot vapor. Such equipment can be used without excessive exposure to the operator, but a considerable number of poor practices, as listed by Horowitz,[4] can result in exposure beyond the recommended limit. Benzol (benzene), carbon tetrachloride, carbon disulfide, and methanol are other industrial solvents that may cause serious illness if not used under properly controlled conditions.

Gases.—In general, potenially hazardous exposure to gases is not obvious in occupational environments. For example, a visit to a gasoline engine test room may fail to indicate the presence of a moderate carbon monoxide hazard. Where carbon monoxide may occur by leakage from a pipe line, or by impingement of a gas flame upon a cold surface with resultant incomplete combustion, or by its use as a reducing gas in a heat-treating department, inquiry should be made into the occurrence of headache among the employees such as would result from moderately elevated concentrations over a number of hours or throughout the day. In addition, the possibility of accidental liberation of high concentrations that may result in asphyxiation should be kept in mind.

These two elements of hazard apply to exposure to a number of other gases. The more prominent symptom from moderately excessive exposure to hydrogen sulfide is irritation of the eye rather than headache, but the danger of rapid asphyxiation is even greater than that from carbon monoxide. Experience has shown that the odor of hydrogen sulfide is no safeguard against excessive exposure, because even brief exposure to sufficiently high concentration results in the loss of the ability to smell this gas.

A number of gases are brought into plants in cylinders in the form of liquids under pressure. These include hydrogen fluoride, used in certain oil-refining processes and in the chemical industry; hydrogen cyanide and methyl bromide, both used for fumigation and for other purposes; and chlorine, widely used for bleaching, in water treatment, and as a bactericide. Other toxic gases include ozone, nitrogen dioxide, and sulphur dioxide.

Dermatitis-Producing Materials.—The phase of the survey dealing with dematitis-producing materials may best start with the industrial nurse who probably will be well informed of the incidence of dermatoses. For example, if no cases from cutting oils and compounds have come to her attention, this source of dermatoses may require no further investigation, but, if numbers of minor cases with an occasional serious case have occurred, this situation should be thoroughly investigated. Attention should be given to washing facilities, soaps and cleansers used, and the availability of hot water. Personal washing procedures as well as other measures such as protective creams and equipment should also be checked.

In addition to solvents, innumerable other primary irritants and sensitizers cause skin affections. Wherever there is skin contact with primary irritants, which may include not only strong acids and alkalis in an electroplating department but even dishwater in a plant cafeteria, there may be some incidence of dermatitis. Skin contact with such materials should of course be avoided, though this is difficult in some operations.

Among the many sensitizers, exposure to those involved in the preparation of synthetic resins and in the manufacture of plastics is worthy of note. The effect on the skin may be caused by contact either with dust or with gases liberated during these processes.

Where waxes are used for impregnation of electric condensers or for wire and cable insulation, inquiry should be made as to whether these are chlorinated naphthalene or diphenyl compounds. If so, suitable precautions (often listed by the producer) should be followed.

Pathogenic Micro-Organisms.—A number of occupations involve exposure to pathogenic micro-organisms, through their incidental introduction into lacerations. In packing houses, measures to avoid brucellosis and psittacosis should be noted. In plants that handle imported animal products, such as hair, bristles, wool, and hides, investigation should be made of the need for sterilization of these materials and, if in order, the method used. Workmen in these plants should be told what an anthrax pustule looks like and impressed with the need for immediate medical attention for such a lesion.

Other Materials.—Materials other than those falling within the foregoing classifications should not be overlooked. Examples of such materials are those capable of inducing cancers, including chromium compounds (lung) beta-naphthylamine and benzidine (urinary bladder), and certain polycyclic hydrocarbons that may be present in coal tars and in certain high-boiling catalytically cracked oils (skin). Surveys of industrial exposure to the cancerogens should be supplemented by epidemiological investigations. A single case of cancer hardly proves a cause-and-effect relationship where exposure to a suspected cancerogen is involved, but incidence of such cases significantly in excess of that occurring in the general population would point to the occupational exposure as a possible cause.

Hazardous Conditions

In addition to hazardous materials, observations should include hazardous conditions. These may be covered under the following headings.

Excessive Noise.—Exposure, particularly of long duration, to excessive noise levels may cause diminished acuity of hearing. Although sufficient data are not yet available on which to specify a precise level of sound of a given frequency that can be taken as a maximum acceptable level, certainly those noise conditions where one must shout within an inch or two of the ear to make oneself heard should be noted in a survey of potentially injurious conditions. The physician, upon finding such conditions, should recommend that a study be made of the noisy environment to determine whether the intensities at existing frequencies are excessive and, if so, to determine whether practical noise-reduction measures can be taken. He might also recommend that an audiometric examination program be instituted.

Extremes of Atmospheric Pressure.—Extremes of atmospheric pressure include the high pressures encountered in foundation and tunnel construction, and in diving operations, and the low pressures of flying at high altitudes. Foundation and tunneling operations under pressure tend to be among the more hazardous.

It is likely that a full-time or part-time physician will be connected with such construction operations. Other physicians in the area may be called upon because of some temporary unavailability of the physician normally responsible, or in event of an accident causing a number of serious injuries. Also their patients may be engaged in such work. Accordingly it is desirable for physicians in the area to visit the project, become informed on compression and decompression schedules, and become familiar with the physical examinations given new workers and with instructions to workers such as checking with the physician before going under pressure in case of a coryza or ear block. Particularly where high pressures are used, the physician should become completely informed on operating conditions before he decides to enter a pressurized area. It would appear prudent for only the younger physician to do so.

In aviation medicine, it is now generally accepted that physicians should be familiar with the effects of low pressures and of too rapid subjection of the body to pressure changes.

Low pressures from high-altitude construction or mining operations are not ordinarily within the purview of most physicians. It is assumed that physicians at operations in such locations will be informed about the physiological aspects of working and living under low pressures—also about the decrease in maximum acceptable concentrations of gases, dusts, and toxic materials, as larger volume of the thinner air must be respired.

Extremes of Temperature: Heat.—In many plants the problems of heat in summertime are no different from those in nonindustrial environments generally. Since the evaporation of perspiration causes cooling of the skin, usually the better the air movement, the greater the comfort. Although high humidity in itself creates no harmful effects, it does limit the rate of evaporative cooling of the skin and can be expected to intensify the effects of high temperatures.

Many plants have local "hot spots," such as ovens, heat-treat baths, and furnaces, that cause excessive exposure to radiant heat as contrasted with heat carried by convection, or hot air. In the steel, glass, foundry, and other industries where processing is built around large-scale melting operations, control of radiant heat is a major problem.

A given amount of heat transferred to a man will have the same effect regardless of the means by which it reaches him—convection, conduction, or radiation. But the control of radiant heat is totally different from the control of the others. If a man is subjected to radiant heat, air movement over the man will not reduce his heat load. Shielding with some reflective material such as aluminum may be required.

The physician should become acquainted with the high-temperature occupations in a plant. Workers with certain circulatory defects should be placed elsewhere. Since long-term physiological effects of working in heat do not seem to be serious and acclimatization is a very real factor, the physician would ordinarily refrain from recommending the alternating of workers between hot and normal-temperature operations.

An increase in the body temperature and pulse rate results from exposure to extreme heat. Since these effects are alleviated fairly promptly on removal to cooler areas, the physician should note whether such areas are available and utilized as required. If an air-conditioned rest room can be provided, recovery is considerably more rapid.[5] When the pulse rate does not decline sufficiently during a rest period in a cooler area, more effective control measures should be recommended.

In hot occupations the physician should observe whether an adequate water supply, with salt, is available for the prevention of heat cramps and exhaustion. Salt is usually taken in tablet form. Several varieties are sold, but the enteric-coated or impregnated type seems the most satisfactory. A cooled, salted water supply is sometimes used. One teaspoonful of table salt per gallon of water is adequate. Thirst is not an accurate indicator of how much water a man needs when working in extreme heat. His fluid loss will usually exceed the replacement induced by thirst. It has been said that one benefit of salt tablets is that they result in a man's drinking more water than would otherwise be the case.

Extremes of Temperature: Cold.—Exposure to extreme cold may occur in meat-packing plants, in deep-freeze food producing and storage operations, and in flying at high altitudes. Provision of proper clothing is the principal factor to be noted. It has been stated[6] that acclimatization to cold has not been satisfactorily demonstrated. An investigation[7] of a group of 66 workers engaged many years in preserved-meat manufacture in cold rooms maintained at 0 to 2C showed a high incidence of chronic muscle and joint pains, and of upper respiratory tract involvement. Inquiry should be made of these possible manifestations of the effects of cold by the physician concerned with such exposure.

Ionizing Radiations.—Ionizing radiations are finding increasing applications in industry. Inquiry should always be made as to whether radioisotopes or x-ray units are being used or whether it is contemplated they will be introduced. Some years ago industrial radiology was limited principally to the use of radium or x-ray for making radiographs of welds and metal castings for detection of flaws. Today a considerable number of radioisotopes are employed for a variety of purposes. Cobalt-60, a powerful gamma emitter, may be used instead of radium for radiography or it may be the source of gamma radiation in recording devices for liquid levels, or in a pipe-thickness gauge. Beta emitters such as phosphorus-32 may be found in thickness gauges for application of rubber coating or in milling of aluminum foil. Even alpha emitters have an industrial use where polonium-coated bars remove static electricity from printing press rolls and other machinery where static interferes with production or safe operation. Radium also continues to be used for this latter application. The risk of inhalation or ingestion of radioactive materials, particularly alpha emitters, should be checked. Radioactive sources and devices utilizing ionizing radiations can be used with safety where adequate precautions are observed.

The physician need not be an expert in the intricacies of ionizing radiation, but he should inquire into the schedule of monitoring exposure to radiation, and review the records of radiation levels within occupied areas and of personal monitoring devices. If exposure should exceed accepted values, he should call to the attention of management the seriousness of the injury that in time may develop. Factors involved in the proper handling of radioisotopes are outlined in a paper on surveying industrial plants for safe use of these materials.[8]

Illumination.—In making a survey of any occupational environment, the adequacy of illumination should be observed. This would include intensity for a given operation and area, together with quality of illumination. This latter factor includes contrast, lack of glare, and proper brightness ratios, in respect to both artificial and daylight illumination. It is not contemplated that a detailed illumination survey will be undertaken by the physician. If his general observation indicates that the illumination is inadequate, the plant management should be referred to publications on industrial illumination[9] and advised to have an illumination survey made. In connection with the relationship of illumination to the visual demands of tasks, attention should also be directed to an adequate eye-examination program, and to suitable eye-protection equipment as well.

Harmful Operations

Repeated Motion.—Injury may be caused by repetitious movements. Attention should be given to operations that may lead to bursitis and synovitis. Information may be obtained from the plant nurse as to whether such conditions have occurred and, if so, at which operations. The physician may be able to make pertinent suggestions for adapting the operation to the physiological and anatomic limitations of the human body.

Vibration.—Compressed-air-driven hand tools are widely used in industry. In many plants the intermittency of the operation or other factos have prevented difficulty. If there has been some incidence of "white fingers" or if these tools are used routinely, reference may well be made to a paper by Dart[10] that covers this condition from the viewpoint of a practicing industrial physician. Heavy pneumatic tools such as jack-hammers reportedly may cause injury to elbow joints, but in this country cases have been few.

ACCIDENT HAZARDS

Operations and Conditions.—If the survey is made in company with the safety engineer, more attention may be given to accident hazards. A check list of operations and conditions to be noted is given by Blake.[11] Unsafe acts of workers account for a greater number of injuries than do environmental conditions and machines, but both factors are involved in the majority of accidents. Information on accident hazards and their control can be gained by a review of the accident experience of the plant and through the plant survey, and also by attending plant safety committee meetings.

SANITATION

General.—The American Standard on Sanitation[12] serves as a guide to general sanitation facilities. The physician should obtain information as to the state and local code requirements. Adequate maintenance and proper use of these facilities should be emphasized. Where difficult-to-remove materials get on the skin, the physician should learn what is provided for skin cleansing and in addition should observe what is actually used. Many a case of dermatitis is caused by use of solvents and harsh abrasive cleaners, even in plants where proper washing facilities and cleaning agents are provided.

Food Handling.—Whether food handling is directly under the plant management or is the function of a catering service, the physician should observe the methods utilized. If foodstuffs are prepared outside the plant premises, the survey should extend to such locations. Methods of refrigeration and of keeping hot foods above the temperature of bacterial germination should be noted. One should inquire into use of foodstuffs after they have been standing in serving areas during mealtime. Garbage disposal should be checked. The storage and use of pesticides in and around food handling and storage areas should be inquired into carefully.

Not only is sanitation of importance in in-plant food handling areas, but also the nutritional adequacy of foods served by the cafeteria and selected by the employees should be checked. It is difficult to change eating habits, but, where food served appears to be nutritionally inadequate, this should be investigated and then proper recommendations made to management. A threefold approach might be suggested through offering balanced meals; making them attractive; and educating personnel in food selection, particularly those greatly underweight or overweight, as well as the diabetics and others who have to watch their diet carefully.

Hazard Evaluation

The general survey of a plant will disclose some operations where hazardous materials are used under obviously safe conditions. Other operations may as obviously be hazardous and call for a recommendation to management that control measures be instituted.

In many instances potentially hazardous operations may be in progress that may or may not cause injury, depending upon the severity of the exposure. Control measures may be costly and management may be reluctant to incur such expense just to "be on the safe side," especially where competitors may not be adding the expense of such control to the cost of their product. In such a case, the question of whether a hazard actually exists may best be answered by recommending that the plant avail itself of expert professional survey services, which may include tests for atmospheric contaminants or of such biological materials as blood or urine, and recommendations for methods of hazard control based on their experience and technical findings.

Such services are available through official departments of industrial hygiene or occupational health in most of the highly industrialized states and in certain of the larger cities and counties. Private sources of these services are available and include a number of the larger casualty insurance companies, full-time consultants, and various professional and research organizations in the field of industrial health, including a number at universities.

RECORDS OF CONDITIONS IN OCCUPATIONAL ENVIRONMENT

After the survey of the industrial environment, the physician should report to management his observations and recommendations. It would also be helpful to the physician to prepare his own record for his use concerning job requirements and health hazards in the plant.

This record should include the potentially injurious materials used or otherwise present; something of the intermittency or duration of exposure to them; and whether the exposure was normally under good control, obviously requiring control, or in need of technical study for its evaluation. The operations involving the potentially hazardous materials or conditions should be listed. A graphic means of associating hazardous materials and conditions with operations or departments consists of a chart on cross-section paper with the materials and conditions along the ordinate, operations or departments along the absicissa, and notations at the intersections indicating existence of the hazard at a given operation or department.

Control Methods

The survey of the plant should include a consideration of control measures, both medical and engineering, which are or should be followed in maintenance of a healthy work force and healthful working environment. It is not proposed that the physician include engineering control as part of his activities. However, an understanding of the engineering factors involved in the control of health hazards will enhance his appreciation of the over-all health aspects of plant operation. The more common control methods are as follows.

MEDICAL CONTROL

Preplacement Examination.—The physician should ascertain the scope of the preplacement examination of all applicants for work and of special examinations of employees who are to be placed in an occupation involving exposure to some hazardous material. For example, employees to be placed in occupations involving exposure to pneumoconiosis-producing dust should be given a chest x-ray and those to be exposed to toxic substances should be given the same clinical tests that will later be used in periodic examinations, to provide base-line values.

Periodic Examination.—The physician should also ascertion which special procedures are included in periodic examinations of employees in hazardous occupations and the interpretations of the findings. If the findings point to possible health impairment, inquiry should be made as to what conditions in the plant are to blame. The intervals at which these special procedures are conducted should be determined by the severity of the hazard and modified as the hazard is brought under control. The interval between chest x-rays should be related to the period required for the development of dectectable changes.

Where a medical control program has been set up by one physician, it is advisable that another making a survey of the plant discuss his observations with that physician.

ENGINEERING CONTROL

Purpose.—The physician making a plant survey has a proper interest in engineering control measures for a number of reasons. The decision of the physician in recommending the placement of a worker at a given operation or retaining him at his accustomed occupation may depend upon the engineering control measures. The physician may have completed an initial x-ray survey of a foundry group and among the core finishers noted one man with arrested tuberculosis. As foundry work is considered by many a physician to be a laborious, hot, dusty occupation, the first thought on reading the x-ray may be that this man may better be placed in some other industry. Consultation with the safety engineer or industrial hygienist or personal survey of this employee's workplace may disclose that his job is conducted while he is at a bench equipped with well-designed local exhaust ventilation, obviously resulting in no appreciable exposure to dust. On the other hand, if an employee subject to asthma is exposed to an organic dust to which he is allergic, and the only feasible control measure is a filter-type respirator (adequate protection for the man's fellow workers), the physician might well recommend that this man be placed in a more suitable location in the plant.

The interest of the physician in engineering control serves as a stimulus to the production and maintenance departments for provision of adequate control measures. The production superintendent is occupied with getting out the product; plant maintenance departments have a backlog of work that a foreman or superintendent is pushing to get done. Provision for control of health hazards is often deferred to the next day, and the next. The physician, in observing the state of control measures, might note that the elbow in an exhaust pipe was eroded and leaking, and find an explanation for the recurrent nosebleed of the chrome plater. When the physician emphasizes need for repairing the ventilating system through the proper channels, it is probable that action will be taken promptly.

Types of Control Methods.—A number of categories of engineering control measures may be applied to reducing to safe levels exposure to hazardous materials. Where substitution of a less hazardous material is feasible, this should be done, for example, toluene for benzene as a paint diluent.

Alteration of method may serve as a control measure. This may involve a minor change such as installation of a motor-operated hoist to replace manual handling of baskets at a vapor degreaser or a major change such as replacement of beehive kilns with tunnel kilns for abrasive wheel calcining. In the latter case, the dust exposure is appreciably decreased and, in addition, efficiency of operation and quality of product are improved.

Isolation has application at many operations. One of these is the use of radioisotopes in well-shielded enclosures, with mechanical devices manipulated from the outside.

Ventilation is the most widely used method of engineering control. General ventilation refers to movement of air from an entire room or building. Local exhaust ventilation is usually more effective, since it is designed to capture the contaminating dust or gas before it escapes into the general room atmosphere.

Wet methods may serve as an effective means of dust control in certain operations. This may involve merely the use of garden watering cans to sprinkle the earth floor around a foundry molding area, or the installation of a high-powered water-sand blast for removal of cores from castings in place of the dusty operation of using pneumatic chisels. Good housekeeping, in itself, is an important control measure.

Personal protective devices have a real place as control measures. Although respirators should not be used as an inexpensive substitute for a local exhaust system, they may be recommended for operations where other control methods are not feasible and where there may be a severe exposure for a brief period. They may be used also as a supplement to other control methods. The type of respiratory protective device selected is extremely important and the physician would do well to learn specifically about the applications and limitations of such devices. Where toxic dusts or gases are present, or where the atmosphere is deficient in oxygen, devices approved for the particular exposure by the U. S. Bureau of Mines and as listed in their reports [13] should be used. Personal protective devices also include goggles, hard hats, gloves, plastic sleeves, asbestos leggings, and clothing made of aluminized fabric to ward off extreme radiant heat.

Conclusions

The purpose of this discussion has been to stimulate the interest of the physician in making surveys of plants with which he may be in contact, to suggest the manner in which he should approach such a survey, and to indicate the nature of conditions that should have his attention during the survey.

The facts obtained should influence the nature of the medical examination given workers, and findings of an examination should be interpreted in the light of such information. Care should be exercised in arriving at conclusions until there has been sufficient examination of all the facts. The mere presence of a toxic agent does not necessarily mean that the exposure is excessive or that injury will occur.

Examples of potentially hazardous materials and conditions, and the operations with which they are associated, have been included, but it is urged that the physician consult reference sources for more complete details. This will place him in better position to appreciate what he sees during the survey and help him in constructive discussion with management.

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MEDICINE AT WORK

MEDICINE HELPS SOW A SEED

How could it happen in mid-20th-century America? Yet there it was in the Tennessee agricultural and mining town of 4,000: Over half the people were throwing their garbage out of doors and windows; 9 out of 10 toilets were outhouses; only 6% of the children had teeth in good condition; hundreds of the frame homes were unpainted, poorly heated, and dimly lit.

Some 2,000 miles northwestward, scores of seasonal farm laborers were suffering from malnutrition, although family incomes were as much as $150 to $350 a week from work in the beet fields and fruit orchards of Malheur County, Ore. Most of the pay was being spent in saloons and gambling joints.

Today, four years later, good health is being established in those two communities. Medicine was at work as the changes took place, but other people and organizations also were on the job. Their combined success there and elsewhere crowns a precept that is governing the rural health movement in America: Help the community to help itself to better health.

In that doctorless valley village near Knoxville, a survey team, set up by the Tennessee State Medical Association's house of delegates, conferred with community leaders. Soon an abandoned commissary building was converted into a physician's office, with local labor a major contribution. Equipment was donated, a state public health nurse arrived (part of her salary paid by women's clubs), and a labor union financed medical specialty services.

Meanwhile, in that Oregon community, state health department mobile units went to the migrant farm labor camps with Spanish-speaking nurses. This helped ease away fears and suspicions of the predominantly Mexican-American workers, many of whom had never seen a doctor in their lives. When examinations showed that some needed medical care, nearly every one paid for treatment by physicians in town. School and church authorities offered help with special courses and recreation programs. Many permanent residents personally welcomed the transients. Prizes were given weekly for the cleanest home and cleanest yard. More money is spent now on food, clothing, and medical care. And there is less business in the taverns and at the gambling tables.

Erasing the Skepticism

In those two communities, as elsewhere in rural America, one of the chief factors obstructing healthful living often has been local skepticism of medical progress in general, and of physicians in particular. Perhaps it has been a mistrust based on lack of knowledge of scientific advancements, or lack of contact with nonfarm folk who just do not "talk" the country language.

Just such hindrances to rural health worried Mrs. Charles W. Sewell of Otterbein, Ind., 11 years ago while she was administrative director of the Associated Women of the American Farm Bureau Federation. She feared the situation might be a setup for widespread quackery and for socialized medicine, and so she asked the advice of her family physician in nearby Lafayette, Dr. F. S. "Davy" Crockett (actually a distant cousin of the popularized Western hero). Dr. Crockett for some years also had been concerned about the effect of the postwar shortage of doctors in some rural areas.

Right there in his Indiana home, Dr. Crockett and Mrs. Sewell founded the American Medical Association's rural health program. Today, he heads the A. M. A. Council on Rural Health (and is also A. M. A. Vice-President), and she is on the Council's 10-member lay advisory committee. The advisors include representatives of farm and ranch organizations, rural publications, and agricultural extension services of land grant colleges.

The idea spread, until now there are rural health committees (many with their own lay advisory boards) in 46 state medical associations and scores more at the county medical society level. These cooperative efforts encompass well over 5 million people active in farm organizations and allied rural endeavors. They include the Grange with 1 million members, the American Farm Bureau Federation with 1,600,000 families, and the 4-H Clubs with over 2 million members. These millions are becoming as keenly interested in their special health problems as are the millions in Los Angeles who are concerned with air pollution and the millions in New York and Chicago who are faced with industrial accident hazards and with a high epidemic potential from crowded living conditions.

Health interest in America's hinterland has reached the point where the Iowa University School of Medicine in a few months will open the nation's first department of agricultural medicine. It will be devoted exclusively to problems in health peculiar to farming and the farm home, such as animal diseases affecting man, rural-type accidents, and the effects of pesticides and insecticides. Already, that school is working with the Washington County Medical Association, the state vocational rehabilitation office, and the Iowa and American Heart Associations in an effort to adjust farm folks to heart disease. There are similar programs for rural dwellers with cardiac conditions in Texas and Indiana.

Extension Service Helps Reduce

Not long ago in Maine, a rural county medical society set up a program to advise overweight persons how to reduce. What made the project attractive was that the university extension service joined in to show how to alter clothing to fit a slimmer figure. Now the weight-reduction program is being extended throughout the state. It is just one example of how an extension service often is the farmer's only link to medicine. Through such an agency, rural communities have made their first pleas for help in organizing clinics and asking health advice.

Mrs Charles W. Sewell of Otterbein, Ind , sought the advice of her family physician, Dr. F. S Crockett of Lafayette, in 1945 when she feared for the health of farming communities Together they founded the A M A.'s rural health program, and today they are leaders in it

Such thirst for counsel points to preventive medicine as more essential in rural areas than in any other kind of community. With sanitation and water supply often a matter of individual supervision, with remoteness of medical facilities sometimes placing a premium on personal protection against illness, the rural family poses a preventive health problem all its own.

Mental health in Cedar City, Utah, is now getting the preventive treatment before it becomes a big problem in that farm community. The county chapter of a mental health organization worked with the Utah State Medical Association and with the school board to show films and distribute pamphlets on the subject, and to encourage hiring of a psychiatric social worker for students. All this is helping certain farm people before they need the help of a psychiatrist, according to Dr. R. W. Farnsworth, a local general practitioner who helped organize the program.

Unfortunately, there was no such project in Sutherlin, Ore., last year when a local pastor told a conference of the A. M. A. Council on Rural Health: "We do not have any psychiatrists, and I know of one case where a 10-year-old boy who functions as a two-year-old is receiving treatments from a chiropractic physician." It is at Council conferences of this sort (the next is scheduled for March 7, 8, and 9 in Louisville, Ky.) that hundreds of physicians meet with hundreds of rural area representatives to relate their problems—and their successes at cooperation.

Doctors as a Community Force

Merely spending time with nonmedical groups in farm communities is shown to be a responsibility in the rural health movement. More often than not, it can be a heartening responsibility, according to Dr. B. L. Masters of Fremont, Mich. Two years ago he visited the office of his county ministers' association to ask advice on his plan to introduce sex education in the farm community's public schools. "To this day," he told an A. M. A.-sponsored study conference at Purdue University last October, "those clergymen still talk in awed tones about the fact that a doctor came to *them* for advice."

Dr. Wyatt Norvell of New Castle, Ky., tells about a colleague's wife who attended a rural PTA meeting where members were ready to decide to ask the local public health department to give Salk vaccine to all children in the community. The physician's wife suggested it was a job for private practitioners instead. So she wound up as the project's committee chairman—and helped coordinate just such a change in plans, in which the serum was given also to those unable to pay.

Just as the American farmer has evolved from a plowman to a combination business manager, meteorologist, mechanic, agronomist, accountant, and veterinarian, so has the "country doctor" of a quarter-century ago grown to the stature of expert general practitioner in many phases of medicine. Scientific advances in agriculture have been just as extensive and rapid as in medicine. Physicians are sharing some of the farmer's problems—helping him in matters of sanitation, nutrition, safety, and the new devices and chemicals on the rural scene. Meanwhile, the farm organizations are helping in health—sponsoring blood banks, safety drives, hospitalization plans, and chest x-ray drives.

Rapport, after 11 years, is now reaching such encouraging proportions that barriers of impersonality are falling left and right. At one recent Midwest meeting of physicians and farmers, the audience grinned in amused agreement, and then grinned at one another, as the speaker commented: "We have a lot in common —rugged independence, high overhead, and freedom from the 40-hour week."

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION
Edited Under the Direction of the Board of Trustees

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Subscription price . . *Fifteen dollars per annum in advance*
Cable Address . . . . "Medic, Chicago"

ATOMIC WAR AND PEACE

Atom-splitting appeared to most people, until 1945, an unrealistic activity to occupy the imagination of professors addicted to the use of quaternions, tensor calculus, and non-Euclidean geometry. However, its overwhelming possibilities were impressed on every literate person in that year by the losses of human life at Hiroshima and Nagasaki. Developments since then have made it clear to all that atomic energy could wipe out the human race unless ways were found to control it. Atomic scientists in particular expressed their consternation at the gruesome consequences of their wartime researches, and many resolved that every effort must be made thereafter to develop peacetime uses of atomic energy. A question that must have remained unuttered in some minds was whether applications of atomic energy to the problems of the physician and the engineer might eventually save enough lives to equal the 160,000 to 480,000 lost in 1945.

Since that time, an incredible amount of constructive work has been done by scientists applying the new knowledge of artificial radioactivity in every field of research. Some conception of the magnitude of their output can be gained by perusing a few issues of the biweekly *Nuclear Science Abstracts*. A considerable fraction of this output relates to biology and medicine. But the question whether these constructive endeavors are keeping pace with military developments is still discussed. In 1955 Japanese investigators claimed that the United States had 2,500 to 3,000 atomic bombs and 25 to 30 hydrogen bombs, as compared with 300 to 500 atomic bombs and 10 to 15 hydrogen bombs in Russia. Has this impressive accomplishment in the military sphere been equaled by the accomplishments of industrial engineers, biologists, and physicians?

Encouraging thoughts on this point are suggested by the appearance of an extraordinary series of 16 volumes representing the proceedings of the International Congress in Geneva, August, 1955, entitled "Peaceful Uses of Atomic Energy." This series contains important contributions from the great laboratories of both hemispheres. Several volumes deal with the legal, administrative, physical, and geological aspects of atomic energy; several deal with the world's requirements for energy, the construction of power reactors, and many technical aspects of reactor engineering. Two volumes deal with applications in research, industry, agriculture, physiology, and biochemistry. Volumes 10 and 11 were reviewed in THE JOURNAL, November 24, page 1266; they are entitled, respectively, "Radioactive Isotopes and Nuclear Radiations in Medicine" and "Biological Effects of Radiation."

These books contain papers from India and Portugal, Argentina and Norway, Romania and Brazil, and many other countries. A contributor from Japan notes that his country now receives radioisotopes from Canada, the United Kingdom, and Holland as well as from the United States. Two North American authors describe an "accidental critical assembly excursion"—an unintended burst of gamma and neutron radiation from a water-moderated reactor—that endangered four workers; this account is paralleled by a report on two workers injured in a mishap with an experimental reactor in Russia. Perhaps equally significant is the fact that the country from which a given contribution came cannot always be guessed from the name of the author: Marcovich turns out to be from France, Parhon from Romania, Bora from India, Shapiro from Norway, Frank from Russia, Cohen from the Netherlands, Marinelli from the United States, Suppinger from Switzerland, and Brull from Belgium. The fields of research show no signs of division by nationalistic lines, and research that stands out by reason of abstruseness or ingenuity or dramatic interest is as likely to come from one country as from another. As a feat of book-making in the technical sense, these volumes also constitute a most heartening example of international cooperation. The work of innumerable secretaries, linguists, editors, typesetters, proofreaders, and others has succeeded in erasing all traces of the limitations and peculiarities of expression that might have been expected in contributions from so many countries in so many languages. It is evident that efforts to save human lives unite humanity and that medical research especially brings people together in combat against a common enemy.

These books do not yet afford a proof, to be sure, that nuclear energy in 11 years of application since 1945 has saved as many lives as were sacrificed in the two fateful days, August 6 and 9, of that year. But they certainly suggest that a tally should become possible and that a day when the total of lives saved becomes equal to the total of lives already lost will arrive. When that epoch is passed, modern man will have demonstrated his ability to handle the two-edged weapons that were placed in his hands by the discoverers of x-rays, radium, and artificial radioactivity.

ORGANIZATION SECTION

CONGRESS ON MEDICAL EDUCATION, FEB. 10-12

At the annual Congress on Medical Education and Licensure to be held at the Palmer House, Chicago, Feb. 10-12, the program will center around the problems of graduate medical education for general practice.

Last year's co-sponsored program with the Advisory Board for Medical Specialties was so successful that it was decided to have another such program during the 1957 Congress. This program will be conducted as a symposium. In addition, papers on the subject will be read, followed by short statements by representatives from the various specialty areas as to "What Should Constitute Graduate Medical Education for General Practice Today." Also, there will be a question-and-answer period.

On Monday, Feb. 11, the program will be devoted to undergraduate medical education. At that time, Dr. Herman L. Weiskotten, who is retiring at the end of the year as Chairman of the Council, will deliver his final address. Outstanding leaders will also present various approaches in an effort to answer: "Why are thoughtful medical educators so restless and dissatisfied today?" The Monday afternoon session will be on problems of postgraduate medical education. On Monday evening the Federation of State Medical Boards will hold the annual banquet, and on Tuesday, Feb. 12, the program will be devoted to the Federation of State Medical Boards. Its program is centered on "Reevaluation of the Licensing Examination."

EXHIBITS BY YOUNG SCIENTISTS AT NEW YORK MEETING

The two high school students winning top American Medical Association awards at the National Science Fair next spring will be invited to be guest exhibitors at the A.M.A.'s Annual Meeting June 3-7 in New York City. Dr. Alphonse McMahon, Chairman of the Council on Scientific Assembly, will serve as chairman of the A.M.A. judging committee at the fair. The A.M.A. awards, two first and two honorable mentions, are presented for the best exhibits in the basic medical sciences as an encouragement to scientifically talented students to enter the study of medicine.

About 800 persons will attend the National Science Fair in Los Angeles, May 9-11, featuring an expected 340 student exhibitors. More than 250,000 high school students now are building exhibits for the 1957 preliminary fairs sponsored by community groups interested in the development of young scientists.

The National Science Fair has increased in size from 13 supporting regional fairs in 1950 to the 170 fairs expected to send finalists this spring. A considerable part of this growth is due to stepped-up activity by medical societies in sponsoring or aiding local fairs. The A.M.A. House of Delegates noted this expanding participation and urged even greater support of science fairs by medical societies in a resolution adopted at the 1956 Annual Meeting. Information concerning the organization of a local high school science fair is available from Science Clubs of America, 1719 N Street, N.W., Washington, D. C.

TOWNSPEOPLE HONOR PRESIDENT-ELECT ALLMAN

Hundreds of townspeople turned out recently to honor Dr. David B. Allman of Atlantic City, N. J., who will take over the presidency of the American Medical Association at the New York session next June. Dr. Louis A. M. Krause, Baltimore, archaeologist, the principal speaker and a close friend of Dr. Allman, selected "Religion and Medicine" as the theme of his address. He paid tribute to President-Elect Allman, saying that "The title of another honor adds nothing to the worth of one who already is himself an honor to all his titles." Among many congratulatory telegrams received that evening was one from President Eisenhower, which read in part: "I congratulate you on your achievements as a physician and on your election to the highest office of the American Medical Association. This is a great responsibility and honor. I extend to you my best wishes for a successful administration."

FILM ON DEAFNESS ADDED TO A. M. A. LIBRARY

A story depicting the problems and education of a deaf child is portrayed in a 16-mm. sound film, which may be obtained from the Film Library of the American Medical Association. Entitled "Susan's Wonderful Adventure," this 29½ minute color film was produced for the Clarke School for the Deaf in Northampton, Mass., to help create a better understanding between deaf persons and those with normal hearing. The story covers about 14 years in a deaf child's life.

SURVEY OF HILL-BURTON PROGRAM

A study of the Hill-Burton Hospital Construction Program now being made by the Council on Medical Service of the American Medical Association will cover the first 10 years of the program's operation. It has been undertaken to determine to what extent the original objectives are being fulfilled, what effect recent progress in medical and hospital care may have had on these objectives, and what changes, if any, might be suggested to improve the program. Recent amendments to the Hill-Burton program include provisions for diagnostic and treatment centers. State medical associations have been asked through a brief questionnaire to report observations to the Council. Individual physicians, also, may have suggestions to offer. If so, such information should be sent directly to the Council's Committee on Medical and Related Facilities.

MEETING OF THE COUNCIL ON SCIENTIFIC ASSEMBLY, OCT. 21

The Council on Scientific Assembly met on Oct. 21, 1956, to arrange the program for the New York Meeting. Among other matters the following actions were taken:

It was voted to cooperate with the Council on Foods and Nutrition in arranging for the presentation of the Goldberger award and the Goldberger lecture at each Annual Meeting.

It was voted to cooperate with the Department of Public Relations in the selection of award winners at the National Science Fair and in the presentation of the first two award winners in the Scientific Exhibit at the New York Meeting.

A Session on Allergy to be held at the New York Meeting under the Section on Miscellaneous Topics was arranged, with Dr. Clarence Bernstein, Orlando, Fla., as Secretary.

A meeting of the Association for Research in Ophthalmology with the Section on Ophthalmology at the New York Meeting was authorized.

A request was made to the Board of Trustees for a committee to evaluate the efficacy of the various parts of the Scientific Program in regard to graduate medical education.

The Council offered its services to the Board of Trustees in studying the facilities of various cities for annual and clinical meetings.

The method of making awards in the Scientific Exhibit was discussed at length, with several recommendations for future consideration.

The Council met with the Section Secretaries and the Section Representatives to the Scientific Exhibit on Oct. 22. It was voted that:

General registration at the New York Coliseum will begin Sunday, June 2.

General scientific lectures will be given Monday morning and afternoon and Tuesday morning.

Section meetings will start Tuesday afternoon, June 4, and continue to Friday noon, June 7.

Arrangements in the New York Coliseum will accommodate the Scientific Exhibit, color television, and meeting rooms for eight sections. The other 13 sections will meet in nearby hotels.

Special features in the Scientific Exhibit include a group of exhibits on perinatal mortality with a question-and-answer conference arranged by the Section on Obstetrics and Gynecology and the Section on Pediatrics, an exhibit on pulmonary function testing with a question-and-answer conference arranged by the Section on Diseases of the Chest, an exhibit on fresh tissue pathology under the auspices of the Section on Pathology and Physiology, and physical examinations of physicians by the Section on General Practice. In addition, there will be the usual Fracture Exhibit and a Special Exhibit on Nutrition with a question-and-answer conference.

The New York Coliseum will be closed to guests of the Association on the mornings of Tuesday, Wednesday, and Thursday, June 4, 5, and 6. On these mornings, physicians only will be admitted to the Technical Exposition, the Scientific Exhibits, color television, and the meetings of the four Sections, which are being held in the Coliseum at that time.

COUNCIL ON MEDICAL SERVICE

A STUDY OF MATERNAL MORTALITY COMMITTEES

This is part 5 of a series of articles by the Committee on Maternal and Child Care of the Council on Medical Service reviewing the organization and operation of maternal mortality study committees. The purpose of this specific study is to obtain information that may be utilized in the preparation of guides that in turn may be helpful in the development and operation of maternal mortality committees in other areas of the United States. The descriptive material to follow is concerned with the Maternal Health Committee of the Michigan State Medical Society. (Part 6 will describe the activities of the Maternal Welfare Committee of the Wayne County Medical Society; this study is an integral part of the statewide program but is modified in some respects in order to better meet the local needs.)

Michigan Maternal Health Committee Study

History.—The study of maternal deaths in Michigan dates back to the early years when the Bureau of Maternal and Child Health of the Michigan Department of Health was established. The first study, covering the period July, 1926, to January, 1929, was made, with the approval of the Michigan State Medical Society, under supervision of the director of that bureau. At the same time, a similar study was conducted in Detroit. Since no report was published, the study received little recognition.

In 1933, the Maternal Welfare Committee of the Michigan State Medical Society was organized under the leadership of physicians dedicated to improving maternal health services and reducing maternal deaths. Up to the time of the inauguration of the present statewide program in 1950, this committee conducted numerous surveys and educational programs and promoted refresher courses in obstetrics throughout the state. During the same period, local studies of maternal deaths were conducted for various lengths of time in Detroit, Grand Rapids, Pontiac, and Flint. This state medical society committee became known, in 1949, as the Maternal Health Committee, and, in 1950, in cooperation with the Michigan Department of Health, it began the statewide study of maternal deaths. Now in its seventh year, the study is definitely accepted as a proper joint function of the medical society and the health department. The purpose of the study is primarily educational; it is directed by and for physicians in their efforts to improve maternal care. The objective, of course, is the reduction of maternal mortality and morbidity in the state.

Members.—All areas of the state were represented on the Maternal Health Committee, and appointments are made by the president of the state medical society on the recommendation of the chairman. The director and the obstetric consultant of the Maternal and Child Health Division of the Michigan Department of Health are members. Other members of the committee include an anesthesiologist, a pathologist, a cardiologist, and five general practitioners. The remaining members—approximately 20—are obstetricians. Many of the members have been reappointed each year: thus there are some who have been on the committee for over 15 years. Within the Maternal Health Committee are subcommittees on study, evaluation, and publications. In addition, a group of 18 regional consulting obstetricians, all of whom are board certified and several of whom are committee members, are officially designated as collectors of study data.

Scope of Study.—Deaths of women who are known to be pregnant or deaths occurring not more than 90 days post partum are defined as maternal deaths and are included in the study. The committee is not concerned with nonmaternal deaths, and, therefore, this term is not used in the committee's study. The maternal deaths are classified as due to either obstetric or nonobstetric causes. The maternal mortality rate includes only those maternal deaths classified as due to obstetric causes.

Classification as to obstetric or nonobstetric cause of maternal death is based upon whether the cause of death was directly related to the pregnancy or its obstetric management. Deaths from hemorrhage, for instance, are categorically classified as due to obstetric causes, whereas most cases of heart disease are categorically classified as due to nonobstetric causes. If, however, obstetric management of a patient with heart disease was at fault, the death is classified as obstetric. Deaths due to anesthesia during delivery are classified as obstetric, because, if the patient had not been pregnant, she would not have been given the anesthesia; such deaths, therefore, belong in the category of those due to obstetric management. Deaths from infections, such as poliomyelitis and tuberculosis, are classified as nonobstetric, whereas deaths in certain cases of pneumonia and most septicemias and infections due to abortion are classified as due to obstetric causes. In the broad classification of toxemia, only those cases of death from essential hypertension with superimposed preeclampsia or eclampsia are classified as obstetric, while those deaths from essential hypertension per se and diseases of the genitourinary tract, such as acute nephritis, chronic nephritis, and pyelonephritis (unless obstetrically mismanaged), are classified as nonobstetric. There are other less common causes of maternal deaths. Sometimes, in the puerperium, there is sudden death from an unknown cause; sometimes there are incompatible transfusion reactions. Such deaths are classified as obstetric. Less common nonobstetric causes of maternal deaths include various types of malignancies, cerebral vascular accidents, diabetes, accidental deaths, and such isolated causes as idiopathic or thrombopenic purpura and leukemia.

Operation: Agencies and Personnel Involved.—The first step in the operation of the Michigan maternal mortality study program is the direct reporting of maternal deaths to the Maternal and Child Health Division of the Michigan Department of Health by the physicians, hospitals, and local health departments of the state. In addition, the Division of Records and Statistics of the health department, which receives all official death certificates, transmits photostatic copies of those coded as maternal deaths and those on which mention of pregnancy or complication of pregnancy is made to the Maternal and Child Health Division. On receipt of these reports, the division office furnishes identifying information to the appropriate regional consulting obstetricians. The consultants then make arrangements for a complete study of each death.

A method of combined questionnaire-personal visit is used in carrying on the study. The consultant discusses the case with the attending physician, reviews the physician's and the hospital's records, and interviews consultants in the case and hospital personnel. If complete data are not available through these sources, he will make arrangements, through the attending physician, for interviewing relatives of the patient or others.

All pertinent data are recorded on the questionnaire form of the Michigan maternal mortality study. To this is added the case summary obtained from the attending physician as well as the regional consulting obstetrician's summary of the data that he has collected. The latter includes notes on the type of hospital facilities, their adequacy, and the adequacy of the medical records and observations on hospital personnel and their competence. The questionnaire and other summaries and comments are sent back to the office of the Maternal and Child Health Division. There all identifying data are removed, and the coded reports are then ready for distribution to the members of the evaluation subcommittee.

The evaluation subcommittee meets at necessary intervals, reviews each case, and determines whether the death was due to obstetric or nonobstetric causes and whether it was preventable. If the death is classified as preventable, responsibility is assigned to the patient, the physician, the consultant, the hospital, or to any combination of these. The publications subcommittee, in cooperation with the Maternal and Child Health Division and the Statistical Methods Section of the Department of Health, makes the final classifications and prepares the material for presentation to the council of the state medical society for approval prior to publication in the state or other medical journals. In counties, such as Wayne and Oakland, where the local medical societies have maternal mortality study committees, the Maternal and Child Health Division routes duplicates of the completed questionnaire and other related material to that county society committee for its analysis, evaluation, and follow-up action. The original material is forwarded to the evaluation subcommittee of the Michigan State Medical Society. After all evaluations and analyses have been completed, all data are again returned to the office of the Maternal and Child Health Division, where they are safely filed. The summaries of attending physicians and regional consulting obstetricians are filed separately from the questionnaires.

Expenses incurred in these studies are shared by the department of health and the state medical society. The department of health pays the regional consulting obstetricians $25 per case, plus traveling expenses; it pays the members of the evaluation subcommittee an honorarium of $25 per session. The state medical society and committee members take care of the expenses of committee and subcommittee meetings and publication of the material.

Follow-Up.—A detailed report on the Michigan maternal mortality study for the three-year period 1950 through 1952 was published in the February, 1955, *Journal of the Michigan State Medical Society.* The issue was a special maternal health number dedicated to the memory of Dr. Alexander M. Campbell, who had done so much in Michigan toward the improvement of maternal care and services. It contained a complete history of maternal mortality studies in Michigan; the history and philosophy of the hospital consultation and licensing program as conducted by the Michigan Department of Health; and an over-all report on the Michigan maternal mortality study for the three-year period. This latter report included graphs and tables showing causes of death, obstetric and nonobstetric, in six main categories: (1) hemorrhage, (2) infection, (3) toxemia, (4) heart disease, (5) anesthesia, and (6) all other causes. In addition, detailed articles on each of these categories gave a breakdown of the factors associated with that particular main cause of death. Analyses were presented on why particular maternal deaths occurred, with suggestions as to how the cases should have been diagnosed and how more appropriate and effective treatment might have been given. A summary and conclusion followed at the end of each article, stating in brief terms what should be done henceforth to prevent many of these deaths.

TABLE 1.—*Data on Maternal Deaths Due to Obstetric and Nonobstetric Causes* from Michigan Maternal Mortality Study, 1950-1952*

Category	Obstetric Causes	Nonobstetric Causes	Total
Hemorrhage	101	.	101
Infection	43	32	75
Toxemia	63	10	73
Heart disease		28	28
Anesthesia	22	..	22
All other causes†	32	51	83
Total	261	121	382

* From Hersey and Sutton,[1] table 1 with modifications.

† Obstetric: Chorioepithelioma, 6; abortion, 5; puerperal pulmonary embolism, 5; immunization with Rh factor, 3; incompatible transfusion reaction, 2; *delivery with other trauma*, 1; and sudden death from unknown cause in the puerperium, 10. Nonobstetric: carcinoma, 9; cerebral hemorrhage, 7; diabetes mellitus, 5; motor vehicle accident, 4; glioblastoma, 2; *pulmonary* embolism, 2; mesenteric infarction, 2; poisoning, (ergot and magnesium sulfate), 2; deaths from unknown cause, 6; and others, 12

From time to time various articles have appeared in county medical society bulletins, sometimes accompanied by open letters to the medical profession. One such series of letters, signed by the chairman of the Maternal Health Committee, the state commissioner of health, and the president of the Michigan State Medical Society, stated the objectives of the Maternal Health Committee, outlined some of the most frequent causes of maternal deaths, and emphasized certain factors that were considered preventable. They also called attention to the licensing of maternity hospitals, now the responsibility of the Michigan Department of Health, and the establishment of minimum rules and standards in consultation with and with the approval of the Michigan State Medical Society.

Through this type of professional publicity, physicians practicing obstetrics and gynecology and hospital administrators throughout the state have learned of the activities of the Maternal Health Committee and that its study of maternal deaths is not disciplinary in nature but is primarily educational, designed to assist the profession in improving obstetric care. To assist in this, the Michigan Society of Obstetricians and Gynecologists devotes one meeting each year to a review of the studies made by the Maternal Health Committee of the Michigan State Medical Society and the Maternal Welfare Committee of the Wayne County Medical Society.

Another method used by the Maternal Health Committee to stimulate further action by an individual county or by groups of counties is to bring its committee meetings to various parts of the state. Undergraduate and graduate education in obstetrics is also furthered in the two university medical school centers through lectures based upon committee findings and through actual participation programs in which the students discuss special cases. This is feasible since representatives from both medical schools serve on the evaluation subcommittee. A newly formed Maternal Mortality Study Committee in one of the counties (Oakland) is tape-recording the discussion and evaluation of maternal deaths studied by them. This is a new innovation, and the value of its results remains to be seen.

The Maternal Health Committee has not received permission as yet from the Michigan State Medical Society to send follow-up letters concerning the findings of the evaluation subcommittee on maternal deaths to the particular physician and/or hospital involved. In the Wayne County maternal mortality study, however, follow-up letters of committee findings are sent directly to the attending physician, the chief of obstetrics, and the administrator of the hospital in which the maternal death occurred.

Results.—The results of the first study of maternal deaths from July 1, 1926, to Dec. 31, 1928, in the state of Michigan indicated 1,627 deaths in 245,312 live births. This is in contrast to the 271 deaths from comparable causes in 510,341 live births during the three-year period from 1950 through 1952.

Table 1 summarizes the Michigan maternal mortality study for the three-year period in two main categories, obstetric or nonobstetric causes. The footnotes to this table indicate the main causes of those maternal deaths classified as "All other causes." Table 2 gives a comparison between maternal mortality rate based upon the maternal mortality study of the Michigan Maternal Health Committee and the maternal mortality rate as recorded by the Michigan Department of Health, Division of Statistics and Records. The slight discrepancy between the two rates is accounted for by the fact that the figures of the department of health were taken directly from the death certificates, which, in some cases, the Maternal Health Committee found inaccurate as to actual cause of death. Provisional reports based on death certificates for 1955 indicate a maternal mortality rate for the state of 0.3 maternal deaths (from obstetric causes) per 1,000 live births. This reveals clearly the progress that has taken place in the reduction of maternal deaths in the state of Michigan since the inception of the statewide study in 1950. Although the committee has evaluated preventability, statistics on this aspect of their study have not been reported.

It is of interest to note that also in the three-year period 1950 through 1952 the rate of infants saved was only 38% of the number of those mothers who died from obstetric causes; the rate was only 25% of the number of those who died from nonobstetric causes. This infant survival rate is slightly less than the infant survival rate (40.8%) recorded for the 1926-to-1928 study.

Comments and Conclusions.—The Maternal Health Committee of the Michigan State Medical Society in conjunction with the Michigan Department of Health has been confident that the study of maternal deaths would lead to a greater improvement in maternal care than would be possible without such a study. The recent low of 0.3 maternal deaths per 1,000 live births in Michigan would seem to justify that confidence. It is difficult to assess the factors most responsible for these dramatic reductions. The Maternal Health Committee feels, however, that the current study, which began in 1950, has assisted materially in that reduction. The publication of critical analyses of the various causes of maternal deaths has great postgraduate educational value to the practicing physicians throughout the state, as well as to the undergraduates in the medical centers of Michigan. It has also resulted in emphasis being given to alerting the public to the fact that early prenatal care is essential in order to reduce the number of deaths.

To arouse public awareness, the state and local health departments have undertaken specific educational programs. In addition, the Michigan Department of Health, as a part of its responsibility for licensing maternity hospitals and homes, provides advice and consultation to the various hospitals and maternity units needing such service in order that they may be aided in meeting the requirements for a license to operate in Michigan. The direct responsibility for this program has rested with the Maternal and Child Health Division and has been carried out in cooperation with other divisions of the state and local health departments. If minimum standards are not met by a hospital and the hospital is needed in the community, it is given a provisional license that allows it to function as such for a period of one year. These provisional licenses can only be renewed two times, and at the end of that three-year period, if the hospital has not met or complied with all the regulations, the license will be revoked. The Michigan Department of Health has had the active participation of members of the Maternal Health Committee for advice and guidance in this licensing program.

Results, since 1951, indicate what physicians and hospitals have done to improve patient care. In 1952, 114 of the approximately 260 hospitals listed had provisional licenses. The basic philosophy of the department of health on the whole licensing program has been to provide advice and consultation to the hospitals, rather than just to point out what is wrong, so that they will better be able to meet the requirements. In this program the health department has had complete cooperation from the Maternal Health Committee of the Michigan State Medical Society; all have worked together harmoniously to assure that good facilities and services are available for mothers and infants in Michigan.

In the course of the work of the Maternal Health Committee, it has become obvious that autopsies are not performed in many of the cases of maternal death in which the cause of death may be in question. In order to solve this problem, a committee, consisting of three pathologists and three members of the Maternal Health Committee, was appointed jointly by the Maternal Health Committee and the state pathological society. This committee is charged with the responsibility of recommending ways and means by which a pathologist might be made available to any physician in the state who needs the service. It is also charged with the responsibility of exploring the establishment of a registration of maternal tissues and determining how such a registration can be accomplished and where it would be best housed.

From the reports published thus far on the activities and accomplishments of the Maternal Health Committee, and with a minimum of emphasis upon specific instances of preventability and responsibility, much progress has been made. However, the Maternal Health Committee hopes to arrive at a solution as to how a more complete analysis can be presented and made more widely known among those in the profession who are concerned with the care of maternity patients. Therefore, in order to promote greater utilization of current knowledge relative to the management of obstetric complications, the Maternal Health Committee plans to present this survey material in more detail at state meetings, at programs in county meetings, and in more frequent publications in the *Journal of the Michigan State Medical Society* and other medical journals. The committee recommends that legislation be enacted that would result in legal immunity regarding information obtained and conclusions reached in the study of maternal deaths. Such a step would go far in allaying the fears of some physicians who perhaps then would cooperate more fully and would, consequently, receive greater benefits from the study. In spite of the fact that during the years of operating an active study of maternal deaths in the state of Michigan there have been no legal complications, the Maternal Health Committee feels that more improvements will result if legislation is enacted to prevent any possible legal entanglements or fears of such entanglements.

TABLE 2.—*Maternal Mortality Rate per 1,000 Live Births**

	1950		1951		1952	
	Deaths	Rate	Deaths	Rate	Deaths	Rate
Michigan Maternal Mortality Study	84	0.52	89	0.52	88	0.51
Michigan Department of Health	91	0.57	94	0.54	82	0.46

* From Hersey and Sutton,[1] table 2 with modifications

References

1. Hersey, M. S., and Sutton, P. E.: Michigan Maternal Mortality Study 1950-1952, J. Michigan M. Soc. 54:168 (Feb.) 1955.

MEDICAL NEWS

ARKANSAS

Narcotic Violation.—Dr. Spriggs B. Banks, of Forrest City, pleaded guilty in Federal Court, Helena, Sept. 10, 1956, to a violation of the federal narcotic law. On Sept. 24, he was sentenced to a term of two years in custody of the U. S. attorney general and to three-years' probation on completion of the two-year sentence.

Meeting on Surgery.—The Arkansas chapter of the American College of Surgeons and the University of Arkansas Medical Center will hold a question-and-answer panel on surgery and surgical specialties, Dec. 9, at the medical center in Little Rock. Panels will be presented on general surgery, traumatic surgery, urology, and gynecology and obstetrics. Registration fee is $5; registrants will be guests at luncheon, 12:45 p. m., in the medical center cafeteria.

CALIFORNIA

Dr. Katz to Address Cardiac Conference.—Dr. Louis N. Katz, chief, cardiovascular research, Michael Reese Hospital, Chicago, will address the Cardiac Surgical Conference of Mount Zion Hospital, San Francisco, Dec. 15, 10:15 a. m. in Herbst Hall, on "Some Dynamics of Circulation."

Personal.—Dr. Leo J. Adelstein, Los Angeles, has been appointed by Governor Knight as a member of the state board of medical examiners for the term ending Jan. 15, 1960.——Dr. Joseph F. Ross, professor of medicine, University of California School of Medicine, Los Angeles, has been appointed a member of the National Advisory Cancer Council, the surgeon general of the U. S. Public Health Service has announced.——Dr. James L. Dennis, coordinator of resident instruction, has been appointed full-time medical director of Children's Hospital of the East Bay in Oakland. Dr. Dennis formerly was assistant professor of pediatrics and assistant administrator of medical affairs at the University of Texas Medical Branch Hospitals in Galveston.——Dr. Arnold D. Schwartz has been appointed chief of the mental health services of the state department of public health, the first person to occupy this position since the resignation of Dr. Kent A. Zimmerman in May, 1954. Dr. Schwartz has been affiliated with the San Bernardino County Charity Hospital, San Bernardino.——Dr. John W. Brown has joined the state department of public health, bureau of acute communicable diseases. Formerly he was a consultant in infectious diseases for the student health services and the department of occupational health at the Ernest V. Cowell Memorial Hospital, University of California, Berkeley. He is presently a member of the committee on public health and preventive medicine of the National Board of Medical Examiners.

COLORADO

Appoint Dean of Medical School.—Dr. Robert J. Glaser, 38, associate dean of the Washington University School of Medicine, St. Louis, has been appointed dean of the University of Colorado School of Medicine, Denver, to succeed Robert C. Lewis, Ph.D., who retired as dean June 30 after 40 years of service as a member of the medical faculty. Dr. Glaser is scheduled to assume his new post about Feb. 1. He joined the faculty of Washington University School of Medicine in 1945 and currently is associate professor of medicine and associate dean.

CONNECTICUT

Groedel Medal to Dr. Fulton.—At the annual meeting in Chicago, the American College of Cardiology named as the first recipient of the Groedel medal Dr. John F. Fulton, Sterling Professor of the History of Medicine, Yale University School of Medicine, New Haven. The award, given "for outstanding contributions in physiology and history of medicine" is named in honor of the late Dr. Franz M. Groedel, founder of the American College of Cardiology. The silver medal was designed by Dr. Hannibal DeBellis, a trustee of the college.

ILLINOIS

Chicago

Grant for Cancer Research.—The Damon Runyon Memorial Fund for Cancer Research has allocated a grant of $12,000 to the Hektoen Institute for Medical Research of Cook County Hospital, for studies in leukemia under the direction of Dr. Steven O. Schwartz and his associates. This is the second yearly grant that the organization has given the institute.

Courses on Radiological and Health Physics.—The University of Chicago will offer courses in health physics and radiological physics, this winter in the department of radiology. The courses are both two-year programs leading to the master's degree Physicists, biologists, and doctors will participate in the instruction. During the second year of the courses, students will be employed half-time either in the university's Health Physics Service or in the department of radiology.

Fund to Help Disabled Physicians.—Money is presently available in the Dr. Adolph Gehrmann fund for sick or disabled physicians in need of financial assistance or for the widow of any physician for a period of not more than one year after the death of the husband. The fund cannot be used as an old age pension for physicians but must adhere to the statement in the will to help "in his or their attempt to regain health." Inquiries should be made to the Chicago Community Trust, 10 S. La Salle St, Chicago 3 (telephone—FRanklin 2-3356).

In Memory of Kellogg Speed.—At 8 p. m., Dec. 14, the Chicago Orthopaedic Society will present a program honoring the memory of Dr. Kellogg Speed, honorary member of the society and founding member of the American Board of Orthopedic Surgery, who died July 2, 1955. Dr. Arthur H. Conley will have as his topic "Dr. Speed, the Rebel." "Swivel Ball Hip Prosthesis" will be discussed by Dr. Carlo S. Scuderi, "Dislocations of the Shoulder" by Dr. James J. Callahan, and "Various Uses of the Kuntscher Nail" by Dr. Horace E. Turner. All physicians are cordially invited to attend the scientific program, which will be held in private dining room 17 of the Palmer House (telephone RAndolph 6-7500). The meeting will be preceded by dinner at 6:45 p. m.

Writers' Association Award to Dr. Fishbein.—Dr. Morris Fishbein, for many years Editor of THE JOURNAL, is the recipient of the 1956 Distinguished Service award of the American Medical Writers' Association, given annually to a member "who has made distinguished contributions to medical literature or rendered unusual and distinguished service to the medical profession." The award, comprising a plaque and gold medal, wa presented to Dr. Fishbein by the president of the association, Dr Richard M. Hewitt, Rochester, Minn., who formerly was Assistant Editor of THE JOURNAL. The presentation was made at th 13th annual meeting of the association in Chicago, Sept. 28.

Personal.—Dr. Michael H. Boley, clinical assistant professor c
obstetrics and gynecology, University of Illinois College of Medi
cine, has returned from a study and lecture tour through Austri
and Germany. He lectured in German on "Management c
Obstetric Difficulties" before the medical faculty and the sta
of the Frauenklinik of Frankfurt University on May 28 an
before the Faculty and Frauenklinik of Heidelberg Universit
on May 29. On June 7 he lectured on "The Present Status c
the Management of Cervical Carcinoma" before the Frauen
klinik and the Faculty of Medicine in Dusseldorf. Dr. Bole
conducted informal seminars at clinics in both countrie
on postgraduate medical education in obstetrics and gynecolog
in the United States.——The Schering Corporation of Bloomfield
N. J., recently awarded second prize ($250) in its internation

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting contest for medical students to Dr. Paul J. Jorden, Chicago, for his paper on trends in the clinical use of adrenocortical steroids. Dr. Jorden is interning at West Suburban Hospital in Oak Park.

KANSAS

Memorial for Dr. Sudler.—Friends of the late Dr. Mervin T. Sudler, former dean of the University of Kansas School of Medicine, Kansas City, who died on June 22, have announced plans for a memorial. Those wishing to contribute to the fund may send checks to the American Medical Education Foundation, 535 N. Dearborn St., Chicago 10. An attached letter should stipulate that the contribution is for the Sudler Memorial Fund and for the University of Kansas School of Medicine.

LOUISIANA

Fellowships in Tropical Medicine.—The Louisiana State University fellowship program to assist teachers from U. S. medical schools in obtaining practical experience in tropical medicine in the American tropics is now in its second year of operation. The program, conducted by Dr. Henry E. Meleney, research professor of medicine, and Dr. William W. Frye, dean and professor of tropical medicine, has already given 33 teachers the experience of two months in the tropics. The original grant of $80,000 from the China Medical Board of New York, which provided financial support for two years, has been augmented by a grant of $40,000 for the third year. The fellows selected spend two days at the Louisiana State University School of Medicine, New Orleans, in an orientation program before proceeding to Central America or the Caribbean islands for eight weeks.

Personal.—A golden anniversary dinner was held recently at the St. Francis Hospital in Monroe, honoring Dr. James Q. Graves of Monroe on the anniversary of his 50 years in the practice of medicine. Dr. Graves has also served 29 years as a member of the House of Delegates of the A. M. A. Dr. Rufus B. Robins, Camden, Ark., gave the address of the occasion, "Fifty Years of Service." An operating room at the St. Francis Hospital was dedicated to Dr. Graves. The meeting was attended by Congressman Otto Passman of Louisiana, Federal District Judge D. W. Dawkins, and other distinguished guests.

MASSACHUSETTS

Dr. Joslin Honored.—Dr. Elliott P. Joslin, Boston, was decorated with the cravat of the commander of the Legion of Honor by the French government at a recent Lafayette Day reception in the French consulate in Boston.

Society News.—The Massachusetts Medical Society (22 The Fenway, Boston 15,) announces that as of Jan. 1, 1957, Mr. Robert St. B. Boyd will retire as executive secretary. General correspondence will be handled through the office of the secretary of the society, Dr. Robert W. Buck.

Dr. Rock Becomes Emeritus Professor.—Dr. John Rock, Brookline, who has been associated with Harvard Medical School, Boston, since 1922, has retired from the university to become clinical professor of gynecology, emeritus. Dr. Rock, who serves currently as consulting gynecologist and director of the Rock Reproductive Study Center at the Free Hospital for Women in Brookline and as a member of the board of consultants of the Massachusetts General Hospital, established one of the first fertility clinics in this country at the Free Hospital for Women and served as its director for nearly 30 years. He is a former president of the Obstetrical Society of Boston, honorary vice-president of the American Society for the Study of Sterility, and honorary member of the Société Française de Gynecologie. He holds the Lasker award of the Planned Parenthood Federation of America and the Ortho award of the American Gynecological Society.

Dr. Wood Retires.—About 250 friends from McLean Hospital and the Massachusetts General Hospital gave an informal buffet to honor Dr. W. Franklin Wood, Belmont, who has retired as director of McLean. Before coming to McLean he had been affiliated with the Massachusetts General Hospital, Massachusetts Department of Mental Health, Boston Psychopathic Hospital, the Massachusetts Memorial Hospitals in Boston, the Monson State Hospital in Palmer, and the Danvers State Hospital. Dr. Wood has been president and secretary of the Massachusetts Hospital Association and of the New England Hospital Assembly, regent of the American College of Hospital Administrators, and president of the New England Superintendents Club. He is psychiatric consultant at the Massachusetts Department of Mental Health and at the Leslie Junior College in Cambridge and has been appointed school physician at the Belmont schools.

MISSISSIPPI

Grants to Dr. Hardy.—The department of surgery at the University of Mississippi Medical Center, Jackson, has announced the following research grants to Dr. James D. Hardy, chairman of the department: from the National Heart Institute, $34,500 yearly for five years for the development and promotion of departmental research in the cardiovascular field; from the division of research grants, National Heart Institute, $25,000 yearly for five years; from the office of the surgeon general, Department of the Army, $39,902.50, renewal for one year, to study patient reaction to anesthesia, operation, and accidental trauma; from the Mississippi Heart Association, $2,400 for one year, to study methods of prevention and treatment of myocardial infarction.

University News.—The department of surgery at the University of Mississippi Medical Center, Jackson, has added the following faculty members: Dr. William F. Enneking, associate professor of orthopedics, formerly instructor in orthopedic surgery at the University of Chicago School of Medicine; Dr. Curtis P. Artz, associate professor of surgery, formerly director of surgical research, U. S. Army Hospital, Fort Sam Houston, Texas, and clinical assistant professor of surgery at Baylor University College of Medicine, Houston; and Dr. Jorge Rodriguez, assistant professor of surgical anatomy and associate in research, formerly of St. Mary's Memorial Hospital, Knoxville, Tenn. Dr. Wanza B. Inmon, who completed his residency in obstetrics-gynecology at the center in July, has been named instructor in that department.

NEW YORK

Society News.—The annual meeting of the Medical Society of the State of New York will take place at the Hotel Statler, New York City, Feb. 18-21, 1957, in celebration of the society's sesquicentennial. The house of delegates will meet in the same location on May 13-15, 1957.

Appoint Professor of Pediatrics.—Dr. Joseph B. Pincus has been appointed full-time professor of pediatrics at the State University of New York College of Medicine at New York City, Brooklyn, and director of pediatrics at the Jewish Hospital of Brooklyn. Until recently he was clinical professor at the college and part-time chief of pediatrics at the hospital.

Appointed Acting Dean.—Wilfred W. Westerfeld, Ph.D., chairman, department of biochemistry since 1945, has been appointed acting dean of the State University of New York College of Medicine in Syracuse. Dr. Westerfeld will serve until the appointment of a dean. The present dean, Dr. William R. Willard, has resigned to become dean of the University of Kentucky Medical School at Lexington.

Society News.—At the October meeting of the Brooklyn Dermatological Society, Dr. Benjamin D. Erger was elected president, Dr. Samuel B. Frischberg, vice-president; and Dr. Morris J. Rothstein, secretary-treasurer. The society holds its meetings on the second Tuesday of each month at 8:30 p.m. from October to May, at the Brooklyn Hospital Clinic at Ashland Place and DeKalb Avenue, Brooklyn.

Community Honors Price Lewis.—Dr. Price Lewis of Holland Patent, N.Y., was recently honored on the observance of his 50th year in practice when members of the community presented him with the Dr. Price Lewis Scholarship, presently worth $3,600, that will be offered annually to a Holland Patent Central School senior who indicates his intention of becoming a physician. Dr. Lewis, health officer of the Consolidated Health District, serves also as school physician for the Holland Patent Central School.

New York City

Harvey Lecture.—The fourth Harvey Lecture in the present series, "Metabolism in Trauma: The Meaning of Definitive Surgery," will be delivered Dec. 20, 8:30 p.m., at the New York Academy of Medicine, 103rd Street and Fifth Avenue, by Dr. Francis D. Moore, Mosely Professor of Surgery, Harvard Medical School, and surgeon-in-chief, Peter Bent Brigham Hospital, Boston.

Laboratory for Experimental Surgery.—Dr. Godfrey Nurse recently donated to Harlem Hospital $100,000 for the equipment and operation of a laboratory for surgical investigation that will be a unit of the department of surgery. The laboratory will be called the Godfrey Nurse Laboratory for Experimental Surgery. Named as trustees of the endowment are Dr. Aubre De L. Maynard, present director of the department of surgery at the hospital, and Dr. Henry W. Cave, a past-president of the American College of Surgeons.

Society News.—The New York Institute of Clinical Oral Pathology announces that its monthly conference, 8:30 p.m., Dec. 17, at the New York Academy of Medicine Building, 2 E. 103rd St., will be an open meeting to which the members of the medical, dental, and allied professions are cordially invited. Albert Schatz, Ph.D., director of research and professor of microbiology, National Agricultural College, Doylestown, Pa., will lecture on "Introspections of a Soil Microbiologist on the Etiology of Dental Caries."

Alvarenga Prize to Dr. Papanicolaou.—On July 14 the College of Physicians of Philadelphia awarded the Alvarenga prize for 1956 to Dr. George N. Papanicolaou, director, Papanicolaou Research Laboratory, Cornell University Medical College, for his work in the early detection of cancer. The Alvarenga prize, established by the will of Pedro Francisco DaCosta Alvarenga of Lisbon, Portu', an associate fellow of the College of Physicians of Philadel ia, is awarded annually on the anniversary of the death of the stator, July 14, 1883.

Research in Causes of Deafness.—The Alfred P. Sloan Foundation has granted $82,000 to New York University–Bellevue Medical Center in support of a project resulting partially from findings established through a pilot study that the foundation supported at the center. The grant was made directly to the postgraduate medical school, department of otolaryngology, of which Dr. John F. Daly is professor and chairman. The director of the hearing project will be R. Joseph E. Hawkins Jr., Ph.D., Rahway, N. J., who has done extensive research on the effects of antibiotics such as streptomycin and neomycin on the inner ear.

Course in Radium Therapy.—A course in operative radium therapy will be offered at the Queens General Hospital, Jamaica, by the radiation therapy department on nine consecutive Saturdays (9 a.m.–12 noon) beginning Jan. 5, 1957. The program will include the use of interstitial radiation in the oral cavity, radical insertion of radium in the neck, radium therapy in postoperative carcinoma of the breast, use of different applicators in carcinoma of the cervix, of the Heyman applicator in carcinoma of the endometrium, of radium needles in the parametrium, and of radon, iridium-thread, and cobalt interstitial therapy. Apply to Dr. Leonard B. Goldman, Director, Department of Radiation Therapy, Queens General Hospital, 82-68 164th St., Jamaica 32.

Personal.—Dr. John A. Di Fiore has been appointed by Governor Harriman as a member of the medical appeals unit of the New York State Workmen's Compensation Board.——The Haitian government, through its consul general, has made Dr. Harry Katz an officer of the Legion of Honor.——The Public Health Research Institute of the City of New York has conferred the title of director emeritus on Dr. L. Whittington Gorham and named Dr. George K. Hirst acting director.——Dr. Samuel J. Prigal recently addressed the National Institute of Allergy and Infectious Diseases, National Institutes of Health in Bethesda, Md., on "Interrelationship of Allergy and Infection."——Dr. Alexander Brunschwig, professor of clinical surgery, Cornell University Medical College, has returned from a two-weeks' tour in Russia, where he visited surgical clinics, cancer institutes, research centers, and medical schools in Moscow and Leningrad.

State Launches Psychiatric Training Program.—A program for advanced training of psychiatrists in the New York State mental hygiene institutions was launched in September under the joint direction of the State University of New York and the New York State Department of Mental Hygiene. The program provides training for medical staffs of six mental hygiene institutions (Brooklyn, Creedmoor, Kings Park, Pilgrim, and Central Islip State hospitals and the Willowbrook State School) in the metropolitan area in cooperation with the faculty of the State University of New York College of Medicine at New York City, Brooklyn. A similar program is planned for upstate mental hospitals, centered around the state university medical school at Syracuse. Dr. Sandor Rado, recently retired from the psychiatric faculty of the Columbia University College of Physicians and Surgeons and the New York State Psychiatric Institute, is director of the metropolitan area program.

OKLAHOMA

Society News.—Dr. Milford S. Ungerman, Tulsa, has been elected president of the Oklahoma Society of Neurologists and Psychiatrists and the Oklahoma District Branch of the American Psychiatric Association; Dr. John F. Gray Jr., Tulsa, vice-president; Dr. Harold G. Sleeper, Oklahoma City, president-elect; and Dr. Charles A. Smith, Norman, secretary and treasurer.

University News.—Dr. Louis J. West has assumed his duties as full-time head of the department of psychiatry at the University of Oklahoma School of Medicine, Oklahoma City, following his release from active duty with the U. S. Air Force.——Dr. John A. Schilling has been appointed the first full-time head of the department of surgery at the University of Oklahoma School of Medicine, Oklahoma City. Dr. Schilling was assistant professor of surgery at the University of Rochester (N. Y.) School of Medicine and Dentistry before coming to Oklahoma.

SOUTH DAKOTA

Distinguished Service Awards.—At its 75th annual meeting in Aberdeen, the South Dakota State Medical Association bestowed its distinguished service award on Dr. Joseph C. Ohlmacher, dean emeritus of the University of South Dakota School of Medical Science, Vermillion.——At its annual awards banquet the Geneva College Alumni Association bestowed on Dr. Frank S. Howe, Deadwood, one of its distinguished service awards for 1956.

TENNESSEE

Gift to Seizure Clinic.—The new Children's Convulsive Seizure Clinic of the University of Tennessee College of Medicine, Memphis, has received $1,000 from a mother in memory of her son who had epilepsy. The clinic, which began operation in July in the outpatient department of the city of Memphis Hospitals, is directed by Dr. James G. Hughes, professor of pediatrics.

VERMONT

Lecture on Urology.—The University of Vermont College of Medicine, Burlington, will present "Urologic Problems of the Paraplegic" by Dr. Wyland F. Leadbetter, chief, urologic surgical service, Massachusetts General Hospital, Boston, on Dec. 10, 8 p.m. The college invites all physicians to visit its anatomic laboratory, which is open from 8:30 a.m. to 5 p.m. on weekdays; Saturdays, 8:30 a.m. to 12 noon.

VIRGINIA

Inaugurate President of Medical College.—On Dec. 17 at 11 a.m. Robert B. Smith Jr., Ph.D., will be inaugurated as the fourth president of the Medical College of Virginia, Richmond. Dr. Smith has served as assistant president since 1954. The speaker for the occasion, Joseph C. Robert, Ph.D., president of Hampden-Sydney College, will have as his subject "The Healing Arts and the American Way." Greetings to President Smith will be brought from the student body by Archer K. Tullidge, president; from the faculty by Dr. Frank L. Apperly, professor of pathology; from the alumni association by Dr. James T. Tucker, president; from the Virginia institutions of higher learning by Colgate W. Darden Jr., LL.B., president of the University of Virginia; and from the Commonwealth of Virginia by Governor Stanley.

WEST VIRGINIA

Allergy Clinic.—The first free teaching Allergy Clinic to be established in West Virginia was opened in July at the Ohio Valley General Hospital, Wheeling, with Dr. Martin D. Reiter in charge. The clinic will be used for indigent patients, and Dr. Mayes B. Williams, medical director of the hospital, has agreed that interns and residents in medicine may receive training there in this specialty.

Personal.—Dr. Sarah L. C. Stevens, Huntington, has received a citation from the President's Committee on Employment of the Handicapped for "outstanding services" rendered the handicapped in West Virginia.——Dr. Walter J. Riley, a member of the medical staff at Weston State Hospital, has accepted appointment as senior physician at Laurelton State Village, a state training school for mentally deficient females at Laurelton, Pa.——Governor Marland has reappointed Dr. George F. Evans, Clarksburg, a member of the Medical Licensing Board to serve for five years and Dr. Delivan A. MacGregor, Wheeling, as a member of the West Virginia Board of Health for nine years.——Dr. Ward Wylie, Mullens, who has served as a member of the West Virginia Senate for the past several years, has been reappointed to membership on the State Athletic Commission for a term of three years.

GENERAL

Fellowship for Women Physicians.—The Women's Medical Association of New York announces that the closing date for applications for the Mary Putnam Jacobi Fellowship (THE JOURNAL, July 14, 1956, page 1090) has been postponed to Jan. 1, 1957. This fellowship of $2,000 is open to medical women graduates for postgraduate study or research. Application blanks may be obtained from the Secretary, Dr. Ada Chree Reid, 118 Riverside Dr., New York 24.

Awards for Study in Statistics.—The committee on statistics of the University of Chicago offers awards for studies in statistics by persons whose primary field is not statistics but one of the physical, biological, or social sciences to which statistics can be applied. The awards range from $3,600 to $5,000 on the basis of an 11-month residence. The closing date for application for the academic year 1957-1958 is Feb. 15, 1957. Information may be obtained from the Committee on Statistics, Eckhart Hall, University of Chicago, Chicago 37.

Research in Schizophrenia.—Grants totaling $82,900 for 22 research projects on schizophrenia were recently announced by the National Association for Mental Health. The grants were made from a $100,000 fund provided by the Supreme Council, 33rd Degree, Scottish Rite Freemasonry, Northern Masonic Jurisdiction, which is directing the research program through the National Association for Mental Health. In the last 22 years, the Scottish Rite has provided more than $1,100,000 for this continuing research program.

Fellowship Program.—A senior research fellowship program, administered by the National Institutes of Health, U. S. Public Health Service, will provide during the first year for a total of 40 to 50 awards to the nation's medical schools, dental schools, and schools of public health. These awards will be increased by a like number each year for five years until a total of 200 to 250 such fellowships are awarded annually. The awards will be for a maximum of $10,000 a year and may be retained for as long as five years. Only three applications a year may be made by each school. The program is designed to attract and hold able investigators in the preclinical sciences. Requests for information should be addressed to the Chief, Research Fellowship Program, Division of Research Grants, National Institutes of Health, Bethesda 14, Md.

Schering Award Contest.—The Schering Award Committee, Bloomfield, N. J., invites submission of papers for the 1957 Schering award contest, which is open to all medical students in the United States and Canada. A total of $4,500 in cash prizes will be awarded, twice the amount offered in any previous year. A $1,000 first prize and a $500 second prize will be awarded for the best papers on each of the three selected topics: (1) Incidence of Various Types of Cardiovascular Diseases by Age Group in the Male and the Female; (2) Recent Trends in Corticosteroid Therapy for Ocular Disorders; and (3) Recent Advances in the Biochemical Aspects and Treatment of Mental Disease. Literature and entry forms are being distributed in medical schools. Students interested in participating should submit their entry forms by Jan. 1, 1957.

Guggenheim Fellowship Awards.—Fellowship awards totaling more than $1,100,000 were granted to 275 scholars and artists during 1956 by the John Simon Guggenheim Memorial Foundation, established by the late U. S. senator from Colorado, Simon Guggenheim, and Mrs. Guggenheim in memory of a son, John Simon Guggenheim, who died in 1922. The foundation's fellowships are granted to men and women, without distinction on account of race, color, or creed, who have demonstrated exceptional capacity for original research in all fields of knowledge and artistic creation in all the arts. Its fellowship grants are made to citizens of all the American republics, the Republic of the Philippines, Canada, and the British Caribbean area. The 1956 awards included four each in medicine and medical physics, history of science, microbiology, and genetics.

Association of American Spas.—The Association of American Spas is compiling a directory of American spas that is expected to be ready this year. The executive vice-president, Mr. E. V. Syrcher, 5200 Blackstone Ave., Chicago, writes that the association recently adopted a code of standards that requires medical supervision of spas, and that this is the first time "that a group of health resorts has voluntarily imposed on their operations" standards that require medical supervision. This code was formulated by a committee of which Dr. Neil D. Buie of Marlin, Texas, was chairman and of which Dr. Russell W. Lewis, Sulphur, Okla., and Dr. Euclid M. Smith, Hot Springs, Ark., were members. Among other provisions of the code is one that requires each spa to have a medical supervisor who must be a doctor of medicine residing in the community and who must also be a member of the A. M. A.

Abel Award in Pharmacology.—At the banquet of the American Society for Pharmacology and Experimental Therapeutics the John J. Abel Award in Pharmacology was presented to Fred Warren Schueler, Ph.D., then associate professor of pharmacology in the medical school of the State University of Iowa and, as of July, professor of pharmacology and chairman of the department of pharmacology at the medical school of Tulane University of Louisiana, New Orleans. This annual award, a bronze medal and $1,000 donated by Eli Lilly & Company of Indianapolis, is named in memory of Dr. Abel who occupied the first chair of pharmacology in this country at the University of Michigan, which created the first separate department for this discipline. Dr. Schueler is known particularly for his work on the relationship between chemical structure of drugs and their beneficial and toxic actions.

Fellowships for Ophthalmology Residents.—The Guild of Prescription Opticians of America has named the following physicians as recipients of fellowships for ophthalmology residents in its nationwide program: Miles A. Galin, Brooklyn, at the New York Hospital, New York City; Eugene O. Wiggs, Denver, at Johns Hopkins Hospital, Baltimore; Eugenio De Juan, Aliceville, Ala., at Grady Memorial Hospital, Atlanta, Ga.; Robert V. Spurney, Shaker Heights, Ohio, at University Hospital, Cleveland; Andrew J. Gay Jr., Long Beach, Miss., at McMillan Hospital, Washington University, St. Louis; and Robert K. Langley, Toronto, Canada, at the University of Toronto. The stipend is $1,800. Six additional fellows will be named each year until the permanent total of 18 fellowships is reached, to be maintained permanently at this number by new selections each year to replace fellows completing their residencies.

Tobacco Research Program.—According to the 1956 report of Dr. Clarence C. Little, New York, scientific director of the $1,500,000 research grant program being supported by the Tobacco Industry Research Committee, "well over $1,200,000 in T. I. R. C. funds have been granted to more than 55 scientists who, with their colleagues, are participating in . . . scientific endeavor to help in solving important health questions." Referring to the fields of cardiovascular and coronary disease, Dr. Little said "the uncertainties regarding *cause and even treatment* remain innumerable. . . . Whether smoking has any significant part, and indeed, whether such a part may be positive or negative, is only *one of the many areas in* cardiovascular investigation that should be explored. Preliminary study indicates that the physical, emotional, and mental characteristics of people who become smokers may be of more significance than has been so far recognized."

Fellowships in Gastroenterology.—The department of medicine, University of California School of Medicine, announces two fellowships in gastroenterology at the University of California Medical Center, San Francisco. The fellow has the opportunity to learn gastroscopy and sigmoidoscopy and other gastroenterological techniques and has the responsibility of preparing case presentations before the weekly gastroenterology conference. Opportunities are afforded for participating in the activities of the department relating to general medicine and to other subspecialties of internal medicine through ward rounds and conferences in the specialty clinics. This fellowship, equivalent to a second-or-third-year medical residency and approved by the Board of Internal Medicine, carries a monthly stipend of $150. Information may be obtained from Dr. J. Alfred Rider, Assistant Professor of Medicine, Department of Medicine, University of California Medical Center, San Francisco 22.

Award by Goiter Association.—The American Goiter Association offers the Van Meter Prize award of $300 and two honorable mentions for the best essays submitted concerning original work on problems related to the thyroid gland. The award will be made at the annual meeting of the association in the Hotel Statler, New York, May 28-30, 1957, if essays of sufficient merit are presented in competition. The competing essays may cover either clinical or research investigations; should not exceed 3,000 words; and must be presented in English. Duplicate typewritten copies, double spaced, should be sent to the Secretary, [illegible] John C. McClintock, 149½ Washington Ave., Albany 10, N. Y., not later than Jan. 15, 1957. A place will be reserved on the program of the annual meeting for the presentation of the winning essay by the author. The essay will be published in the annual proceedings of the association.

Course on Surgery of Nasal Septum.—A postgraduate course, "An Introduction to Fundamentals of Reconstructive Surgery of the Nasal Septum and External Pyramid," will be presented at the Yale–New Haven Medical Center by Yale University School of Medicine, department of surgery, section of otolaryngology, in cooperation with the American Rhinologic Society and Grace–New Haven Community Hospital, May 11-18, 1957. The course, under the guest direction of Dr. Maurice H. Cottle, Chicago, will consist of didactic lectures, case presentations, cadaver dissections, and observation of operations. Enrollment is limited. Applicants must be diplomates of the American Board of Otolaryngology (or its equivalent for doctors from other countries). Scholarship assistance is available to a limited number of foreign applicants. For information write the Assistant Dean of Postgraduate Medical Education, Yale University School of Medicine, 333 Cedar St., New Haven 11, Conn.

Prize in Industrial Medicine.—The International Prize Nicolo Castellino Fund offers an award of one million lira (approximately $16,129) for an unpublished study on a scientific research subject freely chosen by the candidate. The contest is open to students of industrial medicine who on May 30 were not more than 35 years of age and were not holders of an official university chair. Seven typewritten copies of each entry must be received by registered post at the fund's Secretariat, at Naples Policlinic, c/o Istitúto di Medicína del Lavoro of Naples University (Piazza Miraglia, Naples, Italy) not later than March 31, 1957. Entries, each bearing a *nom de plume*, must be accompanied by a sealed envelope containing the name of the author and bearing on the outside the relative nom de plume. The entrant must submit a declaration confirming that the paper entered is an original unpublished work not previously entered or awarded a prize in other competitions. The prize will be awarded at the 12th International Congress of Industrial Medicine in Helsinki, Finland, in July, 1957.

EXAMINATIONS AND LICENSURE

BOARDS OF MEDICAL EXAMINERS

ALABAMA. *Examination* Montgomery, June 18-20. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery 4.

ARKANSAS:* *Examination* Little Rock, June. Sec, Dr. Joe Verser, Harrisburg.

CONNECTICUT:* *Examination* New Haven, Mar. 12-14 Sec, Dr. Creighton Barker, 160 St. Ronan St., New Haven.

DELAWARE: *Examination* Dover, Jan. 8-10. *Reciprocity* Dover, Jan 17. Sec., Dr. Joseph S. McDaniel, 225 So State St., Dover.

IDAHO: *Examination and Reciprocity* Boise, Jan. 7-9. Exec. Sec., Mr Armand L. Bird, 364 Sonna Bldg, Boise.

KANSAS: *Examination and Endorsement* Topeka, Dec. 12-13 Sec, Dr Lyle F. Schmaus, 872 New Brotherhood Bldg, Kansas City.

KENTUCKY: *Examination.* Louisville, Dec. 10-12. Sec, Dr. Russell Teague, 620 South Third St., Louisville 2

MARYLAND: *Examination* Baltimore, Dec. 11-14. Sec, Dr. Lewis P. Gundry, 1211 Cathedral St, Baltimore 1.

MASSACHUSETTS: *Examination.* Boston, Jan 15-18. Sec., Dr Robert C Cochrane, State Office Bldg., Boston.

MICHIGAN:* *Examination* Ann Arbor and Detroit, June. Sec, Dr E C. Swanson, 118 Stevens T. Mason Bldg., West Michigan Ave, Lansing 8

MINNESOTA:* *Examination* Minneapolis, Jan. 22-24. *Reciprocity* St. Paul, Feb. 12-13. Sec., Dr. F. H. Magney, 230 Lowry Medical Arts Bldg, St. Paul 2.

MISSISSIPPI. *Reciprocity.* Jackson, December. *Examination* Jackson. June Asst. Sec., Dr. R. N. Whitfield, Old Capitol, Jackson

MONTANA: *Examination and Reciprocity* Helena, Apr 2-3 Sec, Dr. S A Cooney, 214 Power Block, Helena

NEBRASKA:* *Examination* Omaha, June 17-19. Director, Mr. Husted K Watson, Room 1009, State Capitol Bldg., Lincoln 9.

NEW HAMPSHIRE: *Examination and Reciprocity* Concord, March 13-14 Sec., Dr. John S. Wheeler, 107 State House, Concord

NEW JERSEY: *Examination.* Trenton, June 18-21. Sec., Dr. Patrick H. Corrigan, 28 West State St, Trenton.

NEW YORK: *Examination* Albany, Buffalo, New York and Syracuse, Feb 5-8. Sec., Dr. Stiles D. Ezell, 23 S. Pearl St., Albany.

NORTH CAROLINA: *Reciprocity.* Charlotte, Jan. 14. Asst. Sec, Mrs Louise J. McNeill, 716 Professional Bldg, Raleigh.

NORTH DAKOTA: *Examination and Reciprocity* Grand Forks, Jan 2-5 Sec., Dr. C. J. Glaspel, Grafton.

OHIO: *Examination and Reciprocity* Columbus, Dec. 18-20 Sec., Dr H. M. Platter, 21 West Broad Street, Columbus 15.

OKLAHOMA:* *Examination* Oklahoma City, June 11-12. Sec, Dr. E F Lester, 813 Braniff Building, Oklahoma City.

OREGON:* *Reciprocity and Examination.* Portland, Jan. 7-9 Ex. Sec Mr Howard I. Bobbitt, 609 Failing Bldg., Portland 4.

PENNSYLVANIA: Examination, Philadelphia, Jan. 7-10. Act. Sec, Mrs Marguerite G. Steiner, Box 911, Harrisburg.

RHODE ISLAND:* *Examination.* Providence, Jan. 3-4. Administrator, Mr Thomas B. Casey, 366 State Office Bl[illegible]

SOUTH CAROLINA: *Examination and* [illegible] Dec. 11-12. Sec., Mr. N. B. Heyward, 1329 Blanc[illegible]

SOUTH DAKOTA:* *Examination* Sioux Falls, Jan. 21-22. Ex. Sec., Mr. John C. Foster, 30[illegible] National Bank Bldg., Sioux Falls.

TENNESSEE:* [illegible] Dec. 19-20. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg, Memphis 3.

UTAH. *Examination* Salt Lake City, July 11-13. Director, Mr Frank E. Lees, 324 State Capitol Bldg., Salt Lake City 1.

[illegible] *Examination and Reciprocity.* Burlington, Jan. 30, Feb 1. Sec, [illegible]

[illegible] *and Reciprocity* Seattle, Jan 14-16 and Jan 12. Sec., Mr. [illegible] ohm, Olympia.

WEST VIRGINIA: *Examination* Charleston, Jan 7-9. Sec, Dr Newman H Dyer, State Office Building No. 3, Charleston 5.

WISCONSIN:* *Reciprocity* Jan. 9. *Examination* Madison, Jan 8-10 Sec, Dr Thomas W. Tormey, Jr., 1140 State Office Bldg, 1 West Wilson St, Madison.

ALASKA.* On application in Anchorage, Fairbanks, Juneau and other towns Sec., Dr. W. M. Whitehead, 172 South Franklin St, Juneau

GUAM *Subject to Call* Act Sec., Dr. S. F. Provencher, Agana

HAWAII: *Examination.* Honolulu, Jan 14-15. Sec., Dr. I L Tilden, 1020 Kapiolani St., Honolulu

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

CONNECTICUT. *Examination* New Haven, Feb. 9, Exec Asst, Mrs Regina G Brown, 258 Bradley St., New Haven 10.

IOWA. *Examination* Des Moines, Jan 8 Sec, Dr Ben H Peterson, Coe College, Cedar Rapids.

MICHIGAN. *Examination* Detroit and Ann Arbor, Feb 8-9. Sec, Mrs Anne Baker, 116 Stevens T. Mason Bldg, Lansing.

MINNESOTA: *Examination.* Minneapolis, Jan. 8-9 Sec, Dr. Raymond N. Bieter, 105 Millard Hall, University of Minnesota, Minneapolis

NEBRASKA: *Examination.* Omaha, Jan. 8-9 Director, Mr. Husted K Watson, Room 1009, State Capitol Bldg., Lincoln 9.

OKLAHOMA: *Examination.* Oklahoma City, April 19-20 Sec., Dr E. F. Lester, 813 Braniff Bldg., Oklahoma City.

WASHINGTON: *Examination.* Seattle, Jan. 9-10. Sec., Mr. Edward C Dohm, Olympia.

WISCONSIN: *Examination.* Milwaukee, April 6. Sec, Dr. W H. Barber, 621 Ransom St., Ripon

ALASKA: *Examination and Reciprocity.* Anchorage and Juneau, first week of February, April, June, August and November. Sec, Dr. C. Earl Albrecht, Box 1931, Juneau.

*Basic Science Certificate required.

GOVERNMENT SERVICES

SELECTIVE SERVICE SYSTEM

February Call for Physicians.—The director of the Selective Service System, Washington, D. C., issued the following notice to the state directors of Selective Service on Nov. 19:

1. The Secretary of Defense has informed the Selective Service System of an anticipated call for 450 physicians for delivery in February, 1957, 250 for assignment to the Department of the Army and 200 for assignment to the Department of the Air Force.

2. It is requested that each State Director of Selective Service submit to this Headquarters a report on the number of physicians who as special registrants are classified in Class I-A or Class I-A-O, examined, acceptable, and available as of November 20, 1956, to fill the expected call, as follows:

(a) Number of Priority I physicians.
(b) Number of Priority II physicians.
(c) Number of Priority III physicians born on or after January 1, 1919, by each year of birth as follows:

1919
1920
1921
1922
1923
1924
1925
1926
1927
1928
1929
1930
1931
1932
1933

(d) *Exclude from this report:*

(1) Physicians who will be 46 years of age or older on February 27, 1957.
(2) Physicians who will be 35 years of age or older on February 27, 1957, and have applied at any time for a commission in one of the armed forces in a medical, dental, or allied specialist category and have been rejected for such commission solely because of physical disqualification.

3. The report requested in paragraph 2 of this advice should be submitted by fastest mail so as to reach this Headquarters not later than December 4, 1956.

Lewis B. Hershey
Director

AIR FORCE

Consultants Visit European Installations.—U. S. Air Force medical consultants left Washington, D. C., Nov. 5 to visit U. S. Air Force medical installations in Europe and to attend the U. S. Air Force in Europe medical conference in Wiesbaden, Germany, Nov. 20-21. The group included Dr. Clarence C. Pearson, of the Mason Clinic, Seattle, and Dr. James J. Callahan, of the Callahan Clinic, Chicago, consultants to the surgeon general in internal medicine and orthopedic surgery, respectively; Col. Don. S. Wenger, deputy director, professional services, office of the surgeon general; and Col. Archie A. Hoffman, chief, consultants group, office of the surgeon general.

Promotion of Senior Officers.—The Air Force has announced the promotion of several senior medical service officers. Olin F. McIlnay, director of plans and hospitalization, office of the surgeon general, and Otis O. Benson, commandant, school of aviation medicine, Randolph Air Force Base, Texas, were promoted from the rank of brigadier general to that of major general. Victor A. Byrnes, director of professional services, office of the surgeon general, and John R. Copenhaver, surgeon, Alaskan Air Command, were promoted from the rank of colonel to that of brigadier general.

NAVY

Dedicate Memorial to Hospitalman.—In a ceremony at Alexandria, Va., Nov. 15, a new high school was dedicated to the memory of Navy Hospitalman Francis C. Hammond, Medal of Honor winner. Rear Adm. Irwin Norman, assistant chief, bureau of medicine and surgery; Capt. Willard Calkins, chief, Medical Service Corps; city, county, and state officials; members of the Virginia Board of Education; and representatives of civic and civilian military organizations participated in the dedication. A native of Alexandria, Hammond was awarded the Medal of Honor posthumously. The citation read in part as follows:

> For conspicuous gallantry beyond the call of duty as a Medical Corpsman, serving with the First Marine Division in Korea on March 26-27, 1953. During a counter-attack against an entrenched and numerically superior hostile force occupying commanding ground on a bitterly contested outpost far in advance of the main line of resistance, Hammond's platoon was subjected to hostile mortar and artillery fire, followed by an assault by enemy troops. Advancing through the veritable curtain of fire to aid his stricken comrades, he moved among the garrison of Marines and, although critically wounded, continued to administer aid to the other wounded throughout an exhausting four-hour period. When the unit was ordered to withdraw, he skilfully directed the evacuation of casualties and remained in the fire-swept area to assist the corpsmen until he was struck by enemy mortar fire and fell, mortally wounded. By his exceptional fortitude, inspiring initiative and self-sacrificing efforts, Hammond undoubtedly saved the lives of many Marines. His valor in the face of overwhelming odds enhances and sustains the finest traditions of the United States Naval Service. He gallantly gave his life for his country.

Hospitalman Hammond's widow and son reside in Alexandria, Va.

VETERANS ADMINISTRATION

Orthopedic Shoe Service for Veterans.—The Veterans Administration announced Nov. 9 that its orthopedic shoe services have been centralized in New York City. The centralization will result in more satisfactory repairs and in savings of about $12 per pair on thousands of new shoes annually furnished veterans with foot disabilities. The orthopedic shoe section of the VA prosthetics center in New York stores the individual lasts and patterns from which orthopedic shoes are made by private contractors for some 10,000 veterans in the 48 states. The section also has started a national repair program for orthopedic shoes. In addition to storing the individual lasts and patterns from which new orthopedic shoes are made, the New York center instructs private contractors in details of construction, checks the shoes after they are made, and sends them on to the veterans.

Now, after receiving instructions and a mailing carton from the VA, a veteran anywhere in the country can mail his old orthopedic shoes to the New York center and within two weeks or less receive them relasted and refinished. This expert repairing, it is said, not only reduces the number of new shoes needed but helps insure that each veteran will receive the correct type of repairs for his particular foot condition.

PUBLIC HEALTH SERVICE

Study of Nutrition in Other Countries.—Dr. Frank B. Berry, Assistant Secretary of Defense, Health and Medical, and his group were expected to return Nov. 21 from a tour of countries in Europe and the Middle East where nutritional problems and dietary deficiencies were studied. Stopovers were made at Paris, France; Athens, Greece; Istanbul, Ankara, and Izmir, Turkey; Beirut, Lebanon; Port Lyautey, French Morocco; Teheran, Iran; Karachi, Pakistan; Asmara, Eritrea; Addis Ababa, Ethiopia; and Tripoli, Libya.

Accompanying Dr. Berry were Rear Adm. Bartholomew Hogan, surgeon general of the Navy; Major Gen. James O. Gillespie, from the office of the Army surgeon general; Major Gen. Harry Armstrong, surgeon in the Air Force; Dr. Arnold E. Schaefer, deputy director, Interdepartmental Committee on Nutrition for National Defense; Dr. Joseph S. Butte, from Oregon State College, Corvallis, Ore., and consultant to the Interdepartmental Committee; Dr. Olaf Mickelsen, of the National Institutes of Health, Washington, D. C.; Dr. Richard A. Kern, from Temple University Hospital, Philadelphia; Dr. Edward A. Churchill, professor of surgery, Harvard University, Cambridge, Mass.

While on this trip the group also surveyed medical care provided for U. S. Military Assistance Advisory Groups (MAAG) in the areas visited. Lieut. Commander Thomas L. Hollis, U. S. Navy, executive assistant to Admiral Hogan, was project officer to the group for the 28-day trip.

DEATHS

Dear, William Richard ⊕ Brigadier General, U. S. Army, retired, Washington, D. C.; born in Hamilton, Va., Dec. 7, 1883; University of Pennsylvania Department of Medicine, Philadelphia, 1906; interned at the Central Dispensary and Emergency Hospital; in 1908 commissioned a first lieutenant in the Medical Corps of the U. S. Army and the following year graduated with honors from the Army Medical School; began his military career as a medical officer at outposts in China and the Philippines; during World War I returned to the United States and commanded Army base hospitals at Camp Lee in Camp Lee, Va., and Fort Wadsworth in Rosebank, Staten Island, N. Y.; at the end of World War I assigned to Germany as the chief surgeon of the American Expeditionary Forces; from 1921 to 1923 medical and sanitary director of the American Relief Association in Kazan, Russia; there he directed relief and public health work for the Hoover Relief Mission; between wars served with the office of the Army surgeon general, Washington, D. C.; in 1927 assigned as assistant professor of military science and tactics at his alma mater, where for five years he was head of the Reserve Officers Training Corps unit; during this period commanded the ROTC summer camp at Carlisle, Pa.; from 1932 to the outbreak of World War II served as surgeon at various Army posts in the United States; in April, 1941, after his promotion to brigadier general, was placed in charge of the Medical Replacement Training Center at Camp Lee, Va.; in 1943 became the commanding general of the Northington General Hospital, Tuscaloosa, Ala., where he remained until retirement Aug. 31, 1946; was awarded the Army Commendation Ribbon and the Legion of Merit; member of the House of Delegates of the American Medical Association in 1931; fellow of the American College of Surgeons; a track star in his youth; died in the Walter Reed Army Hospital Sept. 7, aged 72, of arteriosclerosis.

Noble, Robert Ernest ⊕ Major General, U. S. Army, retired, Anniston, Ala.; born in Rome, Ga., Nov. 5, 1870; Columbia University College of Physicians and Surgeons, New York City, 1899; entered the U. S. Army in 1901 as an assistant surgeon; early military service included three years in the Philippine Islands; honor graduate of the Army Medical School in 1904; from 1907 to 1914 served in Panama Canal Zone, in association with Col. William C. Gorgas in the eradication of yellow fever during construction of the canal; during his assignment there, was detailed to mosquito control work in Puerto Rico and Ecuador, and in 1913-1914 was a member of the Commission to Rand Mines, Transvaal, South Africa, studying the causes of pneumonia; following completion of the Panama Canal returned to Washington and was in charge of Medical Corps personnel; went with the American Expeditionary Force to France, returning in 1919 to become librarian of the Army Medical Library; promoted to brigadier general in 1919 when he became assistant surgeon general; in 1920 became a member of the International Health Board Commission of the Rockefeller Foundation studying yellow fever in West Africa and, when General Gorgas died, became chairman; retired Feb. 8, 1925; awarded the Distinguished Service medal; was a commander of the French Legion of Honor; member of the House of Delegates of the American Medical Association, 1917-1918; fellow of the American College of Surgeons; served as president of the Choccolocco Council of the Boy Scouts of America; for his work with the Boy Scouts won the Silver Beaver and the Silver Antelope; was named by the Anniston *Star* as "Man of the Year" for 1955, honoring a long career of devoted service to his country and his community; died in Fort McClellan Sept. 18, aged 85, of bronchopneumonia.

Hibben, John Severy, Pasadena, Calif.; born in Topeka, Kan., in 1888; College of Physicians and Surgeons, Los Angeles, 1914; an associate member of the American Medical Association; fellow of the American College of Physicians; member of the American Society of Physical Medicine and Rehabilitation; past-president of the American Congress of Physical Therapy; specialist certified by the American Board of Physical Medicine and Rehabilitation; from 1917 to 1922 health officer of Pasadena; a founder of the Woman's Hospital; local physician for the Atchison, Topeka and Santa Fe Railway and the Union Pacific Railway; on the staffs of the Alta Vista Hospital, St. Luke Hospital, and the Collis P. and Howard Huntington Memorial Hospital, where he died Sept. 30, aged 68, of cerebral thrombosis, diabetes mellitus, and hypertension.

Potter, Irving W., Buffalo, born in Buffalo, Nov. 12, 1868, University of Buffalo School of Medicine, Buffalo, 1891, specialist certified by the American Board of Obstetrics and Gynecology, member of the American Association of Obstetricians and Gynecologists; fellow of the American College of Surgeons; an associate member of the American Medical Association; past-president of the Erie County Medical Society and the Buffalo Academy of Medicine; author of "The Place of Version in Obstetrics"; consultant, New York Polyclinic Medical School and Hospital in New York City, Deaconess Hospital, Buffalo City Hospital, Lafayette General Hospital, and the Millard Fillmore Hospital, where he died Sept. 17, aged 87, of uremia.

Gage, George Henry, Rochester, N. Y., born in Benton, April 22, 1880; Columbia University College of Physicians and Surgeons, New York City, 1903; an associate member of the American Medical Association; fellow of the American College of Surgeons and the International College of Surgeons; won the Distinguished Service medal and the Croix de Guerre for service during World War I; member of the staff of the Park Avenue Hospital, where he was for many years president of the board; past-president of the Medical Society of the County of Monroe and the Rochester Pathological Society; died in the Park Avenue Hospital Sept. 12, aged 76, of acute coronary occlusion.

Metcalf, Walter Bradford ⊕ Los Altos, Calif.; born in Marengo, Ill., Jan. 3, 1867; Northwestern University Medical School, Chicago, 1894; member of the Illinois State Medical Society, specialist certified by the American Board of Internal Medicine, fellow of the American College of Physicians; at one time practiced in Chicago, where he was on the faculty of the University of Illinois College of Medicine and on the staff of the Cook County Hospital and consulting physician at the City of Chicago Municipal Tuberculosis Sanitarium; past-president of the Chicago Tuberculosis Association; died Sept. 2, aged 89, of carcinoma of the prostate with metastasis to both lungs.

Judovich, Bernard Davis ⊕ Philadelphia; born in Philadelphia, July 7, 1904; Hahnemann Medical College and Hospital of Philadelphia, 1930; associate in neurology at the Graduate School of Medicine of the University of Pennsylvania; joint author of "Pain Syndromes" and "Segmental Neuralgia in Painful Syndromes", on the staffs of the Hospital of the Woman's Medical College of Pennsylvania and the Graduate Hospital of the University of Pennsylvania, where he was founder and head of the Pain Research Foundation and where he died Sept. 13, aged 52, of myocardial infarction.

Allen, Lloyd Raymond ⊕ Colorado Springs, Colo.; Northwestern University Medical School, Chicago, 1903; veteran of World War I, served as treasurer of the Colorado State Medical Society, on the staffs of the Memorial Hospital, St. Francis Hospital, and the Glockner-Penrose Hospital, where he died Sept. 16, aged 77, after gastric resection for a duodenal ulcer.

Ashley, Samuel Glick ⊕ Chanute, Kan.; University Medical College of Kansas City, Mo., 1908; died in the Neosho Memorial Hospital Sept. 17, aged 74, of cerebral hemorrhage.

Baker, Robert Harper ⊕ Pontiac, Mich.; University of Michigan Medical School, Ann Arbor, 1916; served on the council of the Michigan State Medical Society and in 1955 its president; at one time on the faculty of his alma mater; fellow of the American College of Surgeons; past-president, secretary, and treasurer of

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⊕ Indicates Member of the American Medical Association.

the Oakland County Medical Society; veteran of World War I; on the staff of the Pontiac General Hospital, where he died Sept. 6, aged 64, of cancer.

Ball, James Austin ⚕ Charleston, S. C.; Medical College of South Carolina, Charleston, 1900; served on the faculty of his alma mater; died Sept. 16, aged 81, of acute myocardial infarction.

Berger, Samuel Sylvester ⚕ Cleveland; Western Reserve University Medical Department, Cleveland, 1904; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; member of the board of trustees of the American College of Gastroenterology; on the staffs of the St. Luke's Hospital and the Mount Sinai Hospital, where he died Sept. 18, aged 74, of coronary disease.

Boyer, George Milton, Damascus, Md.; Columbian University Medical Department, Washington, D. C., 1902; veteran of World War I; a trustee of the Damascus School; past-president of the Montgomery County Medical Society; an associate member of the American Medical Association; on the staff of the Frederick (Md.) Memorial Hospital; a director and vice-president of the Bank of Damascus; died Sept. 21, aged 84.

Boylan, Thomas Edward, Fall River, Mass.; University of Vermont College of Medicine, Burlington, 1898; medical examiner for Bristol County district 3; served as a member of the school committee; for many years city physician; member of the board of examining physicians during World War I draft; on the staffs of the Union Hospital, Truesdale Hospital, Fall River General Hospital, and the St. Anne's Hospital, where he died Sept. 29, aged 86.

Bunch, James Ralph ⚕ Nevada, Mo.; National University of Arts and Sciences Medical Department, St. Louis, 1916; fellow of the American Psychiatric Association; veteran of World War I; at one time superintendent of the State Hospital No. 1 in Fulton; on the staff of the State Hospital No. 3, where he died Sept. 29, aged 68, of coronary sclerosis.

Buntin, Hansford H. ⚕ Carlisle, Ky.; Kentucky School of Medicine, Louisville, 1891, served on the county board of health; died in the Good Samaritan Hospital, Lexington, Sept. 2, aged 88, of cancer.

Bush, S. Warren, Parkersburg, W. Va.; Baltimore University School of Medicine, 1901; died in the Camden-Clark Memorial Hospital Sept. 18, aged 89, of carcinoma.

Calvert, William Clinton ⚕ West Orange, N. J.; New York Homeopathic Medical College and Flower Hospital, New York City, 1929; veteran of World War II; member of the Association of Military Surgeons of the United States; physician for West Orange schools; on the staffs of the Kessler Institute for Rehabilitation in West Orange, Montclair Community Hospital in Montclair, Orange (N. J.) Memorial Hospital, and the East Orange (N. J.) General Hospital; died in Cutchogue, N. Y., Sept. 29, aged 53, of cerebral hemorrhage.

Cheves, William Grey, Franklinton, N. C.; Jefferson Medical College of Philadelphia, 1925; served as medical director of the state prison system at Raleigh; on the staff of the Franklin Memorial Hospital in Louisburg, where he died Sept. 10, aged 54, of coronary thrombosis.

Collier, Joel Isham ⚕ Navasota, Texas; University of Texas School of Medicine, Galveston, 1907; died in the Baptist Memorial Hospital, Memphis, Tenn., Sept. 1, aged 76, of coronary occlusion.

Davis, John McMillin, Darlington, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1895; served as county coroner; an associate member of the American Medical Association; died Sept. 3, aged 84, of pulmonary edema and arteriosclerotic heart disease.

Davis, Leonard Henry, Milledgeville, Ga.; Medical College of Georgia, Augusta, 1952; interned at the University Hospital in Augusta, Ga., and the Spartanburg (S. C.) General Hospital; district director of the health department; veteran of World War II; died Aug. 26, aged 29, of a heart attack.

Dill, John Robert, Rising Star, Texas; Memphis Hospital Medical College, Memphis, Tenn., 1906; also a druggist; served as health officer; died in Gorman Aug. 26, aged 80, of chronic nephritis.

Donohue, Michael Joseph ⚕ Antigo, Wis.; Northwestern University Medical School, Chicago, 1898; chief of staff at the Langlade County Memorial Hospital; died Aug. 24, aged 82, of virus pneumonia.

Eddy, John D., Morrilton, Ark.; University of Arkansas School of Medicine, Little Rock, 1902; died Sept. 14, aged 92, of heart disease.

Elkins, Charles Edward, Massena, N. Y.; University and Bellevue Hospital Medical College, New York City, 1903; an associate member of the American Medical Association; veteran of World War I; for many years health officer; died in the A. Barton Hepburn Hospital, Ogdensburg, Aug. 9, aged 79.

Ely, George Winfrid, Pittsburgh; Bellevue Hospital Medical College, New York City, 1894; an associate member of the American Medical Association; veteran of the Spanish-American War; at one time a member of the medical department of the public schools; served on the staffs of St. Francis and the Western Pennsylvania hospitals; died Sept. 18, aged 84, of cerebral hemorrhage.

Fowler, William West ⚕ Dallas, Texas; Memphis Hospital Medical College, Memphis, Tenn., 1903; for many years secretary of the Dallas County Medical Society; served as editor of the *Dallas Medical Journal*; died Sept. 10, aged 84, of coronary occlusion.

Grussner, Alfred Sethell ⚕ Schenectady, N. Y.; Medical College of Virginia, Richmond, 1918; fellow of the American College of Surgeons; veteran of World War I; on the staff of the Ellis Hospital, where he died Sept. 12, aged 63, of acute coronary occlusion.

Heckert, Emerson Monroe ⚕ Sunbury, Pa.; Jefferson Medical College of Philadelphia, 1921; veteran of World War I; on the staff of the Sunbury Community Hospital, where he died Aug. 30, aged 65, of coronary infarction.

Henning, Carl ⚕ Rehoboth Beach, Del.; George Washington University School of Medicine, Washington, D. C., 1905; member of the Medical Society of the District of Columbia and the American Academy of Ophthalmology and Otolaryngology; veteran of World War I; for many years practiced in Washington, D. C., where he was on the staff of the Episcopal Eye, Ear and Throat Hospital; died Sept. 12, aged 76, of congestive heart failure.

Hicks, George Amos, Rochester, N. Y.; University of Buffalo School of Medicine, Buffalo, 1916, member of the Medical Society of the State of New York, served on the staff of St. Mary's Hospital; died Sept. 13, aged 70, of coronary occlusion.

Hilton, George Francis ⚕ Garden Grove, Calif.; Central Medical College of St. Joseph, Mo., 1898, member of the Washington State Medical Association; practiced in Wenatchee, Wash., where he was on the staffs of the Central Washington Deaconess and St. Anthony's hospitals; died Aug. 8, aged 80, of Hodgkin's disease.

Hoke, Samuel Erle ⚕ Meadville, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1927; past-president and secretary of the Crawford County Medical Society; served as director of health services at Allegheny College; on the staffs of the Spencer Hospital and the Meadville City Hospital, where he died Sept. 25, aged 54, of coronary occlusion.

Indovina, Vincenzo, Chicago; Regia Università degli Studi di Palermo. Facoltà di Medicina e Chirurgia, Italy, 1893; on the staff of the Mercy Hospital; died Oct. 11, aged 89.

Iseminger, Sidney Willis ⊕ Bakersfield, Calif.; University of Southern California School of Medicine, Los Angeles, 1941; specialist certified by the American Board of Radiology; member of the Radiological Society of North America and the American College of Radiology; president of the Kern County Heart Association; served as secretary-treasurer and vice-president of the Kern County Medical Society; on the staffs of the Mercy Hospital and the Kern General Hospital; died Sept. 29, aged 41, of myocardial infarction.

Jablow, Harry B. ⊕ Dallas, Texas; University of Louisville Medical Department, Louisville, Ky., 1911; veteran of World War I; died Sept. 23, aged 67, of heart disease.

Keeler, Russell Raudenbush ⊕ Harleysville, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1912; veteran of World War I; died Aug. 17, aged 67, of carcinoma of the tongue with metastases.

Key, Samuel Newton ⊕ Austin, Texas; University of Texas School of Medicine, Galveston, 1910; specialist certified by the American Board of Otolaryngology; life member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; past-president of the Travis County Medical Society; formerly secretary and member of the board of trustees of the Texas Medical Association; on the staffs of the Seton and St. David's hospitals; died Sept. 3, aged 70, of cerebrovascular accident.

Killingsworth, Laura Anna U. Penn, Washington, D. C.; Howard University College of Medicine, Washington, D. C., 1908; for many years on the staff of the Freedmen's Hospital, where she was emeritus assistant in gynecology at the outpatient department and where she died Sept. 20, aged 74, of acute myocardial infarction and hypertension.

ing, Samuel, Warren, Pa.; Hospital College of Medicine, Louisville, Ky., 1902; died Sept. 16, aged 90, of cerebral hemorrhage.

Kirkle, Orval LeRoy, West Sacramento, Calif.; College of Medical Evangelists, Loma Linda and Los Angeles, 1931; died in Oakland Aug. 18, aged 61, of arteriosclerotic heart disease.

Knorr, John Keyser, Jr., Wayne, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1900; veteran of World War I; died in the Lankenau Hospital, Philadelphia, Sept. 18, aged 78, of cerebrovascular accident.

Levitas, George Max, Westwood, N. J.; Long Island College Hospital, Brooklyn, N. Y., 1904; an associate member of the American Medical Association; fellow of the American College of Physicians; past-president of the Bergen County Medical Society; served on the staff of the Hackensack (N. J.) Hospital and on the board of governors of the Bergen Pines County Hospital in Paramus; died Sept. 17, aged 74.

Londergan, James Patrick, Providence, R. I., Georgetown University School of Medicine, Washington, D. C., 1930, member of the Rhode Island Medical Society, veteran of World War II, on the staff of the Roger Williams General Hospital and St. Joseph's Hospital; died Sept. 5, aged 54, of carcinoma of the tongue.

Love, Francis Leonard ⊕ Iowa City, Iowa, State University of Iowa College of Medicine, Iowa City, 1906, served as city health officer; on the staff of the Mercy Hospital, where he died July 21, aged 77, of carcinoma of the sigmoid.

McCoy, Clayton Lloyd, Hastings, Pa., Jefferson Medical College of Philadelphia, 1915; an associate member of the American Medical Association; veteran of World War I, on the staff of the Miners' Hospital of Northern Cambria in Spangler; died Sept. 6, aged 68.

Martin, Claude Alexander, Welsh, La., University of Louisville Medical Department, Louisville, Ky., 1912; an associate member of the American Medical Association, served on the town council and board of health; past-president of the Jefferson Davis Parish Medical Society; veteran of World War I and was awarded the Distinguished Service Cross, also won the French Croix de Guerre with two Silver Stars, the Purple Heart medal, and five battle citations; on the staff of St. Patrick's Hospital in Lake Charles, died Sept. 16, aged 73, of heart disease.

Menzies, Robert Campbell, Chicago; Rush Medical College, Chicago, 1905; died Sept. 23, aged 74.

Michie, Henry Clay, Jr. ⊕ Colonel, U. S. Army, retired, San Antonio, Texas; University of Virginia Department of Medicine, Charlottesville, 1907; fellow of the American College of Physicians; entered the Medical Corps of the U. S. Army in 1911, veteran of World War I; retired Feb. 25, 1946; died Aug. 4, aged 74, of heart disease.

Nelson, John Albert, Sr., Tekoa, Wash.; University of Nashville Medical Department, Nashville, Tenn., 1902, served as city health officer; formerly associated with the Indian Service, died Sept. 17, aged 81, of cardiac decompensation, nephrosclerosis, and uremia.

Nolan, Charles Aloysius J., Brooklyn, N.Y., Long Island College Hospital, Brooklyn, 1924, member of the Medical Society of the State of New York; died Sept. 29, aged 60.

O'Connor, John Vincent ⊕ Woonsocket, R. I.; College of Physicians and Surgeons, Baltimore, 1911; past-president of the Woonsocket District Medical Society; on the staff of the Woonsocket Hospital; died Sept. 14, aged 71, of arteriosclerosis and myocardial infarction.

Parsons, John Purl ⊕ Grosse Pointe Park, Mich.; University of Michigan Medical School, Ann Arbor, 1919; interned at the University Hospital, Ann Arbor; for two years resident in internal medicine at the Massachusetts General Hospital, Boston; formerly on the faculty of his alma mater; past-president of the Michigan State Medical Society; member of the American Academy of Pediatrics and the American Academy of Allergy; died Sept. 17, aged 67, of pneumonia.

Pirrung, Joseph Edward, Cincinnati; Miami Medical College, Cincinnati, 1906; fellow of the American College of Surgeons, veteran of World War I; died in the Veterans Administration Hospital, Lexington, Ky., Aug. 24, aged 73.

Quisito, Joseph Michael ⊕ Trenton, Mo.; Kansas City University of Physicians and Surgeons, Kansas City, Mo., 1932, member of the American Academy of General Practice; veteran of World War II; on the staff of the Wright Memorial Hospital, died Oct 2, aged 50, of heart disease.

Roberson, James Franklin, St. Jo, Texas; Vanderbilt University School of Medicine, Nashville, Tenn., 1886, died in Fort Worth Aug. 9, aged 101, of arteriosclerosis.

Robson, Theodore Thomas ⊕ Seattle; Middlesex College of Medicine and Surgery, Cambridge, Mass., 1917; on the staff of the Doctors Hospital, where he died Sept. 17, aged 69.

Roll, Albert Thomas ⊕ Louisville, Ky.; University of Louisville School of Medicine, Louisville, Ky., 1916; formerly practiced in Puumaile and Hilo Memorial Hospital in Hilo, Hawaii, on the staff of the Veterans Administration Hospital; died in the Jewish Hospital Aug. 23, aged 75, of coronary heart disease and hypertension.

Rosenthal, George ⊕ Cherry Valley, N.Y., Universitat Heidelberg Medizinische Fakultat, Baden, Germany, 1910, died Aug. 23, aged 70, of myocardial infarction and coronary arteriosclerosis

Sellers, Frank Este ⊕ Captain, U. S. Navy, retired, San Diego, Calif., University of Virginia Department of Medicine, Charlottesville, 1901; entered the Medical Corps of the U. S. Navy in 1905; retired Sept. 1, 1939, fellow of the American College of Surgeons, died Sept. 13, aged 80

FOREIGN LETTERS

AUSTRIA

Iron Metabolism.—At the meeting of the Society for Pediatrics in Vienna on June 5, Dr. Weippl described the difference between normal iron metabolism in infants and adults. In the infant the amount of iron stored is constantly increasing. Therefore, the absolute iron requirement (in milligrams) is higher in the infant than in the adult, and the relative requirement (in per cent) is even higher. As illustrative cases, the speaker presented the histories of an infant with masked sideropenia who had no anemia despite a severe deficiency of iron and who made a good response to treatment with iron; an infant with a simple alimentary iron deficiency anemia, which, in children, can be almost normochromic; a child with a severe hypochromic anemia, deficient iron absorption, achylia, and a tendency to relapse; a patient with symptomatic polyglobulism and the tetralogy of Fallot who had an increased erythrocyte count and an increase in the serum iron level (despite cyanosis in such a patient, iron therapy may be recommended to strengthen the performance of the heart); a 4-year-old child with acquired hemolytic anemia who did not respond to any therapy and in whom autopsy revealed an excessive siderosis without evidence of hemochromatosis; and an 18-month-old dystrophic anemic child whose anemia was caused by protein deficiency and who was given protein parenterally and by mouth. In this last patient the weight increased and there was normalization of the iron metabolism. The anemia disappeared, but the increase in erythrocytes led to an iron deficiency.

Epidemiology of Poliomyelitis.—At the combined scientific meeting of the Austrian Society of Microbiology and Hygiene and of the Vienna Pediatric Society in May, Dr. H. H. Radl stated that unusual features in the epidemiology of poliomyelitis in the last two years were the increase in the number of cases of the bulbar form and the large number of cases observed from October to December. In 1955 there was an unusually high percentage of contact cases (42.5%). H. P. Krepler reported on a "house-epidemic" in a children's hospital and particularly in the ward for infants, where seven cases of nonparalytic poliomyelitis—two meningeal, three abortive, and two unapparent—were detected and their cause established by identification of poliomyelitis virus type 1 in the feces and neutralizing antibodies in the serum. The same virus was found in the stools of a nurse. Subsequently, in an adjacent ward for internal diseases, a 6-year-old girl who had been hospitalized for several months became severely ill with bulbospinal poliomyelitis 11 weeks after tonsillectomy. A 5-year-old boy, who had a tonsillectomy at the same time, and a 4-year-old boy, who had one a month later, in the completely separated otolaryngological ward, became severely ill 11 days later with bulbar poliomyelitis. One child died.

H. H. Zischinsky stated that house epidemics of poliomyelitis are rare but have been observed at the Wilhelminen Hospital, where they occurred exclusively in the pertussis ward. The first case was seen in the summer of 1949. At this time, 6 of the 14 children on the ward contracted some form of poliomyelitis. A second epidemic occurred in August, 1955, when four cases of poliomyelitis were found in one pavilion of the department of internal medicine. The patients had been admitted with vague symptoms and were moved after the diagnosis was made. In September, one case of paretic poliomyelitis occurred in this pavilion among the children with pertussis, all of whom had already been hospitalized for several weeks. Careful clinical and spinal fluid examinations did not reveal any evidence of poliomyelitis among the other exposed children. In October, the ward was again filled with victims of pertussis, who remained free of poliomyelitis, but, in November, new victims of pertussis were admitted, after all the previous victims had left, whereupon paretic poliomyelitis developed in a child who had been in the hospital for five weeks. Of the 21 exposed children only 3 escaped infection with the virus. All but the first victim had only mild symptoms and slight changes in the spinal fluid. Investigation revealed poliomyelitis virus type 1 in a nurse. Since no other source of infection was ascertainable for these children, who had been hospitalized for weeks before the onset of their poliomyelitis, it is assumed that the nurse, by taking care of the first victims in August, had become a carrier and thus caused the house epidemic. Since such epidemics have been seen only in children with pertussis, it would seem that pertussis produces a definite predisposition to poliomyelitis and that the house epidemic was favored by the increased opportunity for group contact.

H. P. Kraus stated that he isolated 17 virus strains of type 1 (Brunhilde) from 61 stool specimens of patients and contacts of the two house epidemics reported. This would indicate that the same type of causative agent can be found in epidemics with different courses. The serologic examinations (demonstration of virus-neutralizing antibodies) confirm the types, which were identified by culture. An increase in antibodies could be demonstrated in three children, who had contact with poliomyelitis victims but did not show an increased cell count in the fluid. This suggests that viremia, which occurs in the course of an unapparent infection, does not necessarily lead to infection of the central nervous system.

INDIA

Fellowships for Indian Professors.—Five special fellowships have been awarded to Indian professors by the World Health Organization to study preventive and social medicine at the Harvard School of Public Health. These fellowships form part of the medical education program established by the government and WHO in which the teaching of preventive and social medicine in undergraduate medical courses is to be given greater emphasis.

The Indian Public Health Association.—The Indian Public Health Association has been formed under the chairmanship of the director-general of health services. It will afford a means of communication between the thousands of public health workers throughout the country and will publish quarterly the *Indian Journal of Public Health.*

Soft Tissue Sarcomas.—M. V. Sirsat reported a series of 146 patients with soft tissue sarcomas of the extremities and trunk (*Indian Journal of Surgery,* August, 1956). Fibrosarcomas ranked first in frequency and formed 60.3% of the soft tissue sarcomas. Of these, 75% occurred in patients between the ages of 30 and 50 years (average 38.8). The thigh was the commonest site. Local recurrence was observed in 73.9%, this high rate being due to inadequate initial surgical treatment. Rhabdomyosarcoma of skeletal muscle formed 20.5% of soft tissue sarcomas in this series. Most of these patients were between 41 and 50. It showed a definite predilection for the lower extremity and especially the thigh muscles, which were involved in 30% of the patients. Rhabdomyosarcomas and synovial sarcomas have a poor prognosis. Patients with undifferentiated sarcomas run a rapid downhill course, with early appearance of pulmonary metastases. Other types met with included lipogenic sarcoma, reticulum cell sarcoma, and angiosarcoma. Biopsy helps in planning correct treatment. The line of incision in surgical excision of the tumor must pass at least 3 cm. outside the palpable limits of the tumor at all points.

Lymphangiography in Scrotal Filariasis.—U. S. Arora and co-workers (*Bulletin of the Calcutta School of Tropical Medicine,* July, 1956) reported the use of lymphangiography to determine the presence of lymphatic obstruction and its site, nature, and extent in six patients with scrotal filariasis. The duration of the illness varied from 3 to 14 years. Microfilaria bancrofti was found in the peripheral blood as well as in the lymph aspirated from the dilated scrotal lymphatics in two patients and in two others

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The items in these letters are contributed by regular correspondents in the various foreign countries.

it was found only in the scrotal lymph. Ten cubic centimeters of a radiopaque dye was injected percutaneously into a suitable dilated scrotal lymph vessel. No untoward reactions were noted. The lymphatics were well visualized in all cases. In four patients the filling was unilateral and in the other two bilateral. The presence of obstruction was shown in all by the dilated tortuous intercommunicating lymphatic vessels with regional filling defects. The site of obstruction in all appeared to be at about the level of the superficial inguinal lymph nodes of the side injected.

Health Education.—At the meeting of the southeast Asia regional committee of the World Health Organization in Delhi in September, Lieut. Col. T. C. Puri (India) stressed the importance of health education in southeast Asia, where ignorance, poverty, and other socioeconomic conditions were responsible for so much preventable disease. He said that the school child should receive special priority because he is easily accessible and the school teacher could give the necessary instructions. Through the school child, knowledge of health could be introduced into the home and thence the neighborhood, and when the child grew up he would have a constructive attitude on matters of health.

Medical Services in Assam.—A steady progress in medical services in Assam is recorded in an official report. The number of hospitals and dispensaries has risen from 408 in 1951 to 453 in 1955 and the number of beds from 2,520 to 2,624. Extensive repairs and expansion have been carried out in the five local board hospitals. Provision was made to increase the number of beds in these hospitals from 100 to 200 and to install modern equipment, such as x-ray machines. The five district hospitals were provided with x-ray machines and other modern equipment in the past year. Further expansion by adding 25 general beds and 20 beds for tuberculous patients in each of these hospitals was approved by the planning commission under the second five-year plan. Other smaller hospitals and institutions will also receive necessary aid. The Gauhati Ayurvedic College, the only institution of its kind in Assam, has established a research department. A new training center for auxiliary nurses and midwives has been opened.

SWEDEN

Effects of the Free Sale of Alcohol.—Up to Oct. 1, 1955, spirits were rationed in Sweden, only wine and beer being obtainable without serious restrictions. After this date, Swedes were freely allowed to buy as much alcohol as they pleased. The statistics for the first half year of this experiment show a marked rise in the sale of spirits and the number of arrests for drunkenness. In May, 1955, the number of such arrests was 768, whereas the corresponding number for May, 1956, was 2,272. In Stockholm, the rate of occurrence of delirium tremens has more than doubled, and the public asylum at Beckonberga has been unable to accommodate all the applicants for admission for alcoholism.

Doctors and Journalists at Variance.—Because of growing disagreement between the medical profession and the lay press, the Swedish Publicist Club invited representatives of the medical profession to present their viewpoint and to listen to that of journalists and editors. *Svenska Lakartidningen* for September gives a report of this discussion. Dr. Justus Strom pointed out that the relations between himself and the lay press had on the whole been cordial, but that they had lately been marred by an incident when a journalist had reported on a patient in such a way as to put Strom in a false light. While private medical practitioners are usually left alone by the press, it would seem that as soon as a patient is admitted to a public hospital he is assumed to be public property as far as his news value is concerned. If he is a man of some importance, journalists may inquire about his progress early and often so that an obituary of him can be printed promptly if he dies. This is distressing to both patient and physician. Dr. Erik Husmark suggested that the newspapers put the reporting of medical news on the same footing as that enjoyed by music, literature, and the theater. While these subjects are dealt with in the big papers only by well-qualified reporters, medical matters are often reported by the uninitiated. The journalists and editors for their part referred more than once to the mutual jealousy of physicians and to the suspicion that if one of them appears in the papers his colleagues will suspect him of advertising himself. While a busy surgeon cannot be expected to tell the press on the phone how his patient fares, it would be appreciated if he would let the press know whether the patient is alive or dead and whether he has a serious condition. One speaker referred to setting up a central pool from which all papers could draw their medical news as an impractical plan because reporters by nature fight shy of a pool from which all can draw. Most editors prefer their own sources of information.

Prednisone for Asthma.—From a hospital in Gothenburg comes a report from Dr. Hans Arnoldsson on his experiences with prednisone and prednisolone in the treatment of bronchial asthma. All his 100 patients were severely affected and had failed to recover under conventional treatment, and 56 of them showed radiologically demonstrable signs of emphysema. The dosage was usually 30 mg. daily during the first few days, after which it was gradually reduced to a maintenance dose of 5 mg., which was in most cases sufficient to keep the asthma under control. There were, however, a few patients who needed as much as 10 mg. daily. In 71 patients complete freedom from symptoms was achieved and in 19 appreciable amelioration. No definite clinical improvement could be claimed in the remaining 10. In two patients, however, radiologically demonstrable gastric ulcer developed a month or two after this treatment had been started. Arnoldsson finds that hypertonia and cardiac insufficiency need not be contraindications for treatment with prednisone and that it does not require precautionary measures in respect of sodium and potassium regulation; however, diabetes is a contraindication, and the risk of gastric ulcer must be borne in mind.

Cottage Hospitals.—In *Svenska Lakartidningen* for Sept. 28, Dr Gunnar Redell discussed the influence of modern advances in surgery on the functions of small hospitals classified generically as "cottage hospitals." When surgery was still a comparatively simple matter, an enterprising surgeon might have been justified in performing a laparotomy in a small hospital in a thinly populated area, but to get away from the anachronism of performing major operations in small hospitals today, the functions of each of the smaller hospitals need scrutiny and perhaps revision. A recent memorandum by the Swedish Ministry of Health warns against the building of small hospitals without reference to their special functions. The larger cottage hospitals may be expanded so as to become important surgical hospitals, while others may care for the chronically rather than the acutely ill patient. They should have some observation beds and others for after-care of maternity patients. In industrial areas they may also serve as clearing stations.

UNITED KINGDOM

Mode of Transmission of Micrococcus.—Experiments carried out by Hare and Thomas on nasal carriers of Micrococcus pyogenes var. aureus suggest that this organism is not transported primarily by the expulsion into free air of droplets or droplet nuclei coming from the anterior nares (*Brit. M. J.* 2:840, 1956). Although the nasal carrier is the ultimate source of micrococcic infections, the organism is spread by transfer, in three stages, from the nasal secretions. The first stage is the transfer of the micrococci by hands or by handkerchief or any other object coming into contact with the nose to the skin, clothing, bedding, and other objects in the vicinity of the carrier. The next step is the release of the organism into the air. This may result from friction and the dislodging of dried particles from the skin and hair, from the spattering of water droplets when washing, and from the shaking of clothing on which the organisms have settled. Many members of hospital staffs are carriers of micrococci and dissemination in the afore-mentioned ways may occur anywhere in the hospital. The third step is the transport of infected particles by air currents to other persons in the vicinity. In this manner the micrococci may spread to the anterior nares of other persons and produce the carrier state in them. Highly susceptible tissues, such as the conjunctiva of the newborn child and the fresh open wounds occurring in operating theaters, may become infected. Breathing, coughing, talking, and sneezing expel only comparatively few organisms. Some carriers produce a much greater degree of air contamination from the friction and movement of their clothes than do others. In a hospital, such carriers are probably more dangerous as sources of infection than are persons with micrococcic infections of the skin. If they wear a sterile gown over their ordinary underclothes, they may still cause potentially dangerous degrees of air contamination. Even when wearing a complete set of sterile operating clothes, they may still disseminate micrococci into the surrounding air.

Micrococcic Pneumonia.—According to Hausmann and Karlish, micrococcic pneumonia is becoming more prevalent (*Brit. M. J.* 2:845, 1956). They reported 18 cases of this condition in a series of 122 consecutive patients with pneumonia admitted to a medical unit. The outstanding features in the patients were the severity of the clinical course of the disease and the number of suppurative complications. Only 6 of the 18 patients responded to treatment with penicillin. This observation is in keeping with the general experience that micrococci are becoming increasingly resistant to penicillin. A history of previous pulmonary disease, such as chronic bronchitis, asthma, or recurrent pneumonia, was obtained in over 40% of the patients. The patients in whom penicillin was no longer effective responded to tetracycline and erythromycin.

Pellagra Caused by Isoniazid.—Harrison and Feiwell (*Brit. M. J.* 2:852, 1956) record a case of pellagra developing in a woman given isoniazid for the treatment of multiple sclerosis. She was given 300 mg. of isoniazid daily and 20 mg. of pyridoxine three times a day. The summer was exceptionally warm and sunny, and, after two or three months, she began to complain of burning sensations in the hands and feet. Eventually a typical symmetrical red-brown pellagral dermatitis developed on the hands and feet. At night she was unable to sleep with her limbs covered. Angular stomatitis, another pellagral lesion, was also present. Therapy with isoniazid was stopped, and the patient was given 1 gm. of nicotinamide. Within 18 days the burning pain left and the skin lesions cleared. Although the patient's diet was suspected of being inadequate, it should have been sufficient for normal needs. Therefore, the pellagra was attributed to the isoniazid having produced a nicotinic acid deficiency by a competitive block in one of the enzyme systems utilizing nicotinic acid.

Medical Manpower in Scotland.—The Scottish Committee of the British Medical Association has submitted a memorandum to the Minister of Health on medical manpower in Scotland. The committee said that it could only speak of present trends and could not predict those of the future. There are four Scottish universities, and so far they have trained more physicians than are needed to satisfy the requirements of Scotland. Many of these physicians go to England and elsewhere. For many years the proportion of men and women in Scotland wishing to become physicians has been higher than in the rest of the British Isles. In 1948-1949 there were 2,419 Scottish general practitioners within the National Health Service, 653 specialists, 274 prospective specialists, and 427 junior hospital medical staff. By 1955 these figures had increased to 2,568, 876, 353, and 517 respectively. These physicians serve a population of about 6 million. By far the greatest increase—about 30%—has been in the number of physicians serving in hospitals under the health service. This increase was inevitable, since the amount of service rendered by the hospitals has been increased by 35 to 40%; thus there is no question of overstaffing the hospitals. The committee thinks that the size of the hospital staffs should remain stationary unless there are new developments in medical knowledge and practice. The increase in hospital attendance has not led to any reduction in the general practitioner service. Patients are seeing their physicians oftener, and the numbers referred to hospital must, therefore, inevitably increase. The number of general practitioners in Scotland is probably insufficient, as most family physicians have patient lists that are still too high for efficient service.

The committee estimates that British medical schools will have to produce enough replacements for the total medical force of about 60,000 and enough more to allow for an increase of 10% in the next 10 to 25 years. Admissions of students to Scottish medical schools have fallen by 20%. This is attributed not only to a decline in the number of entrants to the professions but also to more rigorous selection of students. Formerly most students came from professional, including medical, families, but this is no longer so. Physicians are not encouraging their children to enter the medical profession. Many of the professional classes, whose income has not increased to the same extent as that of the working classes, cannot afford to put their children through medical school. The committee thinks, however, that any decline in the number of entrants is only temporary. The factors likely to influence medical requirements are those immediately and directly affecting the practice of medicine and the general level of health in the community. In the first group are advances in the knowledge and understanding of disease processes and in the means of treating or preventing them. The committee deprecates the existence of a system whereby the organization and financing of a medical service depends on an annual parliamentary vote. The money that is forthcoming is usually unconnected with medical needs and has to be determined in advance. This does not make for flexibility and is likely to affect the hospital and specialist services the most.

The committee is not convinced that the increasing age of the population will result in an increased need for medical services. Much of the illness of older persons is preventable, so that, in the future, geriatric services should reduce rather than increase the demand for medical services in older persons. Studies on school children show an improvement in the general level of health in the young. This has been largely due to preventive medicine, and it may be that more physicians will be needed in this branch in the future. More will also be needed for the treatment, and possibly prevention, of psychogenic disorders. It is estimated that the annual number of physicians required for replacement in Great Britain is about 2,200. The figure for 1955 was 2,309. An intake into medical schools of this number does not allow a large margin of physicians to meet the increased demand that the committee thinks will arise in the near future. To produce annually a sufficient number of physicians for that would require an intake of nearly 3,000, this allows for a student failure rate of about 15%. This number is in excess of the present total intake of all medical schools in the British Isles. There is thus no evidence at present that steps should be taken to limit the number of entrants into the medical profession. Long-term requirements cannot be forecast. The situation should be kept under review. If there is any excess number of entrants over demand, the entrance and qualification standards could then be raised.

WORLD HEALTH ORGANIZATION

Disposal of Radioactive Wastes.—A. W. Kenny in the *Bulletin of the World Health Organization* (14:1007, 1956) states that, although the immediate burning of the skin by relatively intense sources of radioactivity has long been appreciated, the fact that smaller sources, producing no immediate visible effect, may cause harm and even death was recognized slowly because the effects did not develop until years after the irradiation and were similar to those of known diseases. In consequence, the pioneer workers developed blood diseases and suffered skin injuries. Even in recent years there have been injuries to the eyes of scientists working with high-energy radiation machines. The fact that no cure or treatment of these diseases is known must make for caution in estimating maximum permissible levels. At the present stage of development of the atomic power industry and of the use of radioisotopes, no particular difficulty is met in achieving these levels by means of conventional methods of waste disposal, except with the high-level liquid wastes, consisting largely of fission products from the chemical processing of irradiated fuel elements, and with contaminated, noncombustible, solid wastes. These wastes must be stored. Fortunately, since the liquid wastes are of small volume, storage is not expensive, but the possibility of leakage to ground waters must give rise to some apprehension when atomic power is widely used. For this reason, methods of fixing the fission products in solid form, e. g., by absorption in clay or by incorporation in cements or ceramics, have been investigated. Alternatively, it seems that a process based on chemical precipitation of the two long-lived fission products, radiostrontium and radiocaesium, might succeed, for the remaining fission products, after storage for 10 to 15 years, would decay to levels that would permit disposal without difficulty.

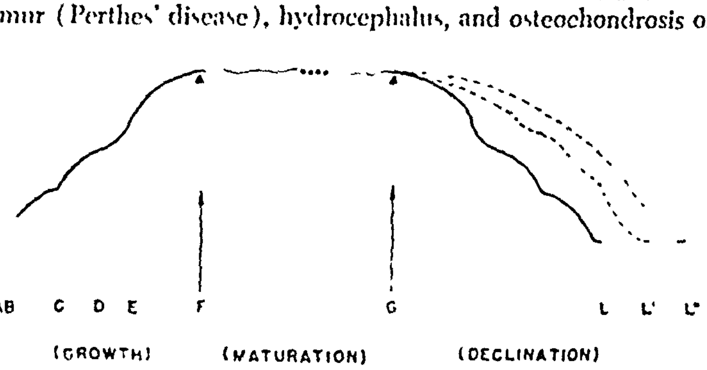
CORRESPONDENCE

GERIATRIC RESEARCH

To the Editor:—The term geriatric research must be better defined or dropped entirely. At present it includes research done in anatomic or pathological categories (myocardial infarction, atherosclerosis, cancer) solely on an age basis. There is rationale for this, since each of the categories included is accentuated in the later years of life in severity and prevalence. However, none of the categories is limited to this period of life and so should not be included comprehensively in geriatric research.

In pediatric research *it* may be possible to find the counterparts of geriatric research. Growth and development clearly belong here. On the gerontologic side of the picture, normal alterations *of function that begin at the close of the mature phase*, that are *attributable only to age*, and *that* are strictly retrogressive (loss of physical agility and muscle tone, bone hardness) would be comparable.

In childhood, liver, spleen, kidney, lungs, bones, blood, and all other body components have abnormalities of action that are limited strictly by puberty *or earlier maturations*: hyaline membrane disease, to the first few days of life; nephrosis, *to the period from 2 to 5 years of age. Osteochondrosis of capital epiphysis of femur* (Perthes' disease), hydrocephalus, and osteochondrosis of navicular (Köhler's bone disease) also appear in normal children within very circumscribed age limits. Susceptibility to infection varies sharply, and the sequelae vary greatly and are as bound by the changes with age. Infants are highly susceptible to streptococcic infection, but the occurrence of rheumatic fever is rare in children under 5 years of age; newborn infants are immune to measles, mumps, and typhoid, but by 6 months of age they have become susceptible to the first and by 2 years of age to the second. It would seem logical that each of these examples, and all the others not given, might be matched at the other end of life. If life were graphed it might be done as illustrated in the figure, taking only the more conspicuous nodes for the purpose.



Graph depicting phases of life

The components A through F represent the growth phase. A-B *represents* the rapid development from the ovum to birth; B-C, from birth to 5 years of age; C-D; 5 to 9 years of age; D-E, 9 years of age to puberty. and E-F. puberty to somewhat more years. possibly to 25. F-G, representing the phase of maturity, although obviously not a flat horizontal line, begins—and ends—vaguely, at different ages in different people. It does not begin sharply at sexual puberty, but later, when height ceases to increase and the forming mind stops indiscriminate absorption and becomes stabilized. It is not ended by a sexual change (menopause) any more than it is begun by one. During the maturation phase the course is up, mentally, and down, physically. The two courses are not widely separated but have this definite digression in their directions.

The ill-defined G *point is a critical one* in preventive geriatrics. It is here that the mature blood vessel begins to lose its vigorous tone and to become too rigid or too impermeable, or both. The nerves, muscles, and all other parts suffer as a result.

G has even a greater variability *in the time of* its appearance than F. It is as if life increases, and then diminishes, in harmonics. The latitude in gestational periods is not great, but perhaps is 10% of the life span to the time of birth. Puberty varies from 9 to 15 years of age in its appearance. This is roughly a 40% difference between normal individuals. The G point varies normally among individuals much more widely than this, and, in the exaggerated instance of the comparison of the times of its appearance in a progeric child 6 years of age to that in a normal adult of 70, it is *several* hundred per cent. Commonly, it is observed that the onset *and rate of aging is one of the most variable* physiological phenomena among mankind. The F-G span has diseases of its own, arterial spasm (notably of the coronaries but also *of* the extremities), thromboses, embolisms, peptic ulcers, and alcoholism are some of these. They may precipitate aging, *they may bring the* G point earlier, but, of themselves, they are not geriatric problems.

Geriatric research should be directed toward the study of phenomena that might be discovered to be as compartmentalized as those known to exist in the pediatric age group. Its objective should be the recognition of the G point, and the postponement of it, by reversing its earliest phases through nutritional, physical, or other simple measures. *Once past it, however, the declination* of the curve G-H-L should be established, its wide variability acknowledged, and the concomitants of its slopes and horizontals learned so that each can be approached separately as well as with the presently conceived, *all inclusive, frontal attack.*

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PERIODIC EXAMINATIONS FOR PHYSICIANS

To the Editor:—Like many other speakers of the American Cancer Society addressing the lay public, I have often endorsed the recommendation of yearly routine health examinations. At times a rather obvious question is asked: "Do doctors and their wives follow this advice?" Many surveys have pointed to early detection as the key and best hope for cure of cancer at present, also *other diseases* have been detected and treated early. I am certain that, like myself, many of our colleagues would be glad to participate in setting aside certain hours for checking our fellow physicians and their wives. Doctors, doubling as patients, may *also help clarify* several unsettled questions of clinical laboratory and x-ray procedures. A special committee might do well to study these *questions* and to define procedures along with methods of compensation of the laboratory for actual expenses. Some physicians hesitate to impose *on* their colleagues by asking *for an* examination. This may or may not be justified, but it is hardly compatible with preservation of good health. Above all, *should* not the profession demonstrate to the public a model system of health checkups practiced on their own members?

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MEDICAL FILM REVIEWS

Fractures of the Leg and Ankle: 16 mm., color, sound, showing time 29 minutes. Produced in 1956 by Churchill Wexler Productions, Los Angeles, for and procurable on loan from Veterans Administration, Central Office Film Library, Washington 25, D. C.

This film presents, in a simple and diagrammatic manner, the skeletal anatomy of the leg and ankle and a sensible and practical outline of the common types of fractures that occur in the shafts of the tibia and fibula and of the ankle malleoli. There is no presentation of a variety of methods of treatment for each fracture. The functional anatomy and the forces by which each fracture is caused are clearly demonstrated. In outlining the open reduction of the fracture of the tibial shaft, it would have been well to emphasize bone grafting, as an added insurance for healing, at the time the fracture was opened. With regard to the position recommended for the immobilization of an eversion ankle fracture, a demonstration of an inversion position of the heel and talus rather than one of a twist of the foot would have been proper. The photography, animation, and art work are outstanding. The film is excellent for a review of functional anatomy and therapy for injuries of the leg and ankle. It is recommended for showing to general practitioners, surgeons, and medical students.

Operative Obstetrics: 16 mm., color, sound, showing time 27 minutes. Prepared by John Q. Adams, M.D., and Ben E. Everett, M.D., University of Tennessee, Memphis. Produced in 1955 by and procurable on loan from Sandoz Pharmaceuticals, Route 10, Hanover, N. J.

This film demonstrates various maneuvers of the forceps commonly used in the practice of obstetrics. The proper application of the Simpson-De Lee forceps is demonstrated, both on an excellent manikin and on live patients in three different types of deliveries: occiput anterior and occiput posterior rotation and breech. The normal third stage is shown as well as the episiotomy repair. The continuity of the film is excellent; however, it would be well to show the placenta as it is inspected and also to show the checking of the fetal heart tones on all three patients instead of only on the last. The photography is fair. The film would be ideal teaching material for medical students, interns, residents, general practitioners, and nurses. However, it is not recommended for specialists.

Home Care: An Approach to the Treatment of Chronic Disease: 16 mm., black and white, sound, showing time 26 minutes. Presented by the Benjamin Rosenthal Foundation, Inc., with the technical assistance of Montefiore Hospital, New York. Produced in 1955 by Information Productions, Inc., New York. Procurable on rental ($10) or purchase ($50) from Health and Welfare Materials Center, 10 E. 44th St., New York 17.

This film presents an effective method of bringing hospital-type care into a patient's home, with the full complement of medical, nursing, and social service. The film shows the effects of such care on patients with cancer, heart disease, asthma, arthritis, and other chronic conditions; it also describes the factors that go into the selection of patients for treatment in a home care program. The roles of the physician, nurse, and social worker are also shown. The results of this type of care on a patient's physical and emotional well-being are described. The film gives a good demonstration of the effective use of home facilities for care and rehabilitation of the chronically ill; however, it is important to emphasize that the teaching facilities were available to the group shown in the film. A discussion guide accompanies the film. It will be of interest to physicians, nurses, social workers, and also to the parents of chronically ill patients.

Excision and Split Skin Grafting of Extensive Pigmented Nevus of Right Upper Extremity: 16 mm., color, sound, showing time 18 minutes. Prepared by Thomas D. Cronin, M.D., and Raymond G. Brauer, M.D., Houston, Texas. Produced in 1955 for and procurable on loan from Eaton Laboratories, Norwich, N. Y.

This film shows an 11-year-old girl who has an extensive pigmented hairy circumferential nevus involving a major portion of the right arm and forearm. She also has other smaller pigmented nevi and an associated scoliosis. The film demonstrates how the large tumor is removed and then covered with a large split thickness skin graft. As fat offers a poor bed for a skin graft, the skin grafting is delayed one week to permit a fine granulating bed to form over the fat. The technique of adjusting and using the Padgett dermatome is shown. The postoperative course is followed, showing the use of a foam rubber pressure bandage to minimize hypertrophy of scar around the grafts. Surgically speaking, the film is well produced and the photography is good. It would be of particular interest to general practitioners and dermatologists in pointing out what can be done with this type of lesion.

NEW FILMS ADDED TO A. M. A. MOTION PICTURE LIBRARY

You Are There: The Tragic Hour of Dr. Semmelweiss: 16 mm., black and white, sound, showing time 25 minutes. Produced in 1955 for CBS Television. Procurable on rental or purchase ($125) from Young America Films, 18 E. 41st St., New York 17 or on loan (service charge $2) from Motion Picture Library, American Medical Association, 535 N. Dearborn St., Chicago 10.

This film, which portrays a significant highlight in man's fight against superstition and ignorance, is one of the series in which the well-known television personality, Walter Cronkhite, brings history to life in a way that makes the viewer feel that "You Are There." In a setting that realistically portrays the dingy, frightening atmosphere of hospitals a century ago, Dr. Semmelweiss is dismissed from his Vienna hospital because of his fight to prevent childbed fever, which, he believes, is due to inattention of the medical profession to sanitary conditions. To see this film is a memorable experience because of its gripping drama, which is, perhaps, most keenly felt by anyone with medical experience but will be appreciated by any mature audience. It is easy to identify one's self with this young doctor who finds himself unable either to become resigned to the abuses he sees or to discover a way to correct them. He sees a young mother brought to a maternity hospital in old Vienna and assigned to a ward where the death rate from puerperal fever is known to be high. She is browbeaten into submission, and the expected tragedy happens—a healthy young mother is lost, and a child is orphaned. So plausible is the action that the ultimate defeat of Dr. Semmelweiss at the hand of well-entrenched politicians, his frustration, and his insanity enlist one's sympathy. This is one of the best films available today as a means of impressing people with the progress that has been made in medicine and in hospital operation. It can be especially recommended for medical students and student nurses.

Embryology of the Ear: 16 mm., color, sound. Presented by the American Academy of Ophthalmology and Otolaryngology with the cooperation of George W. Bartelmez, Ph. D., Carnegie Institute of Washington, D. C., and Franz Altman, M.D., Columbia University, New York. Produced in 1955 by Sturgis Grant Productions, New York. Procurable on loan (service charge $5—each part) from Motion Picture Library, American Medical Association, 535 N. Dearborn St., Chicago 11.

Part I: The Inner Ear: Showing time 30 minutes.

This film demonstrates that the ear can be divided into three parts: external, middle, and inner. The demonstration continues with the inner ear, showing the otic labyrinth, the otic capsule, and the periotic labyrinth.

Part II: The Middle Ear: Showing time 27 minutes.

This film deals with the middle ear and the external ear.

Part III: Blood Vessels—Arteries: Showing time 33 minutes.

The final portion of the film discusses the blood vessels, arteries, and veins, and it ends with a summary of the entire subject. This motion picture represents much detailed observation on the development of the various parts of the ear throughout the various stages. In the film this detailed information has been brought together and presented in a way in which the development can be clearly followed. The amount of material contained here is so great that for the purposes of study the film has limited value. It is to be regarded more as an authentic and detailed record of the various stages of development, a record that can be consulted to best advantage by the student already familiar with most phases of embryology. It is not suitable for showing to medical students, but it should be of great value as an authoritative source of information to those trained in otology or embryology.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Why Drugs Are Not Enough in the Treatment of Tuberculosis. A. R. Allen. A. M. A. Arch. Int. Med. 98:463-466 (Oct.) 1956 [Chicago].

One hundred seventy-one patients with caseous and/or cavitary pulmonary tuberculosis were subjected to a regimen consisting of the administration of streptomycin, aminosalicylic acid, and isoniazid given concurrently and continuously from admission to discharge, with early resectional surgery when indicated. The results of the gastric culture before resection and the culture of a portion of the resected specimens were compared with the results of bronchoscopy and pathology in 168 patients.

Conversion occurred in 84% of the patients by the end of four months of combined chemotherapy with all three drugs, a better conversion rate than can be obtained with only streptomycin and aminosalicylic acid. However, of the 145 patients who were negative on culture before surgery, 12% had positive cultures of their specimens, another 11% had positive smears of their specimens, and 11% had reactivation of their lesions. Thus drug therapy in any combination will not cause conversion in all patients. The types of lesions that are not sterilized by chemotherapy are thick-walled cavities, caseous masses over 2 cm. in diameter, and bronchial stenosis and bronchiectasis. Caseous lesions with a bronchial connection manifested by positive cultures before drug therapy is started are as dangerous as open cavities. Apparently, combined chemotherapy is less effective in extrapulmonary tuberculosis than it is in pulmonary disease. Using equipment and techniques available only in a tuberculosis hospital, i.e., good culture methods, anteroposterior tomographs, and bronchoscopy with right-angle and foroblique telescopes, it is possible to determine which patients will require more than combined chemotherapy alone. If resectional surgery is indicated, it should be performed within three to four months after starting combined chemotherapy. The acid-fast rods found in pathological specimens are viable, virulent tubercle bacilli and if not removed surgically will result in reactivation. Drug therapy is merely a tool in the treatment of tuberculosis, effective for a limited time, and if it is not properly used the patient will have lost the opportunity for successful resection.

The Risk of Tuberculosis in Adrenal Cortex Therapy. J. Charpin and J. Béranger. *Presse méd.* 64:1507-1508 (Sept. 19) 1956 (In French) [Paris, France].

Five cases are described in detail to exemplify the appearance or recurrence of tuberculosis in patients who received cortisone as medication for other conditions. The infection was pulmonary in all cases, but in one it assumed a miliary form, involved the brain, and terminated fatally within two months despite the use of antibiotics. Statistical proof of a relation between the cortisone and the tuberculosis would be difficult because it would necessitate consideration of the relative frequencies of tuberculosis in those receiving and those not receiving cortisone. It is the opinion of the authors that tuberculosis after cortisone is in reality extremely rare; what is striking is the chronological relation and severity of the tuberculosis. They conclude that during cortisone therapy the risk of tuberculosis is practically negligible but that the lungs require watchful care none the less.

Lupus Vulgaris and Fatalities After BCG Vaccination. F. van Deinse. Ztschr. Tuberk. 109:33-40 (Sept.) 1956 (In German) [Leipzig, Germany].

Vaccination ulcers and suppuration of lymph nodes occur after BCG vaccination, but they are a part of the BCG primary complex—a severe form of this complex. Eczematoscrofulous or lichenoid cutaneous lesions also occasionally develop after BCG vaccination. This report is concerned chiefly with the development of lupus vulgaris (tuberculosis luposa) and with fatalities To date, 14 cases of tuberculosis luposa have been reported, 7 in the Scandinavian countries, 5 in Holland, one in Germany, and one in France. In four of these patients cure had not been established at the time the report was made. In view of the millions of BCG inoculations, tuberculosis luposa is an extremely rare complication, and whenever it occurred numerous other children and adults had tolerated the same batch of vaccine without any complications. It seems that an extremely rare individual hypersensitivity is responsible for the tuberculosis luposa reaction

Four fatalities attributable to BCG have been reported from the Scandinavian countries. There was a report from France concerning an infant vaccinated with BCG scarifications, in whom death resulted three months later from suppurating lymph nodes, high fever, and emaciation. No tubercle bacilli could be demonstrated in this infant, and isoniazid therapy was ineffective The author does not believe that this fatality should be ascribed to BCG, although the French authors who reported the case did attribute it to the vaccine. The bacteriological findings in the four deaths reported from the Scandinavian countries seem to indicate that the BCG vaccine was the cause, but the author shows that the cases took a very unusual clinical course, and histological studies revealed no changes indicative of tuberculosis. Thus, although the first impression was that BCG had caused these deaths, closer investigations show that this has not been definitely proved. BCG is highly susceptible to antibiotics, and yet none of these four patients had shown the slightest response, although the cultured organisms had remained sensitive. The author questions the possibility that the diagnosis of tuberculosis can be based on bacteriological findings alone, and suggests that a still unknown, related organism may have been present. Even if the deaths were really attributable to BCG, the number of fatalities is so small, in view of the fact that over 100 million persons throughout the world have been vaccinated with BCG, that BCG vaccination is still the safest method of protective vaccination.

Rheumatoid Arthritis and the Positive L. E.-Cell Phenomenon J. H. Kievits, J. Goslings, H. R. E. Schuit and W. Hijmans Ann Rheumat. Dis. 15:211-216 (Sept.) 1956 [London].

Joint symptoms occur in a large number of patients with lupus erythematosus. If Hargrave's L. E.-cell test could be considered absolutely specific, it would then seem possible to diagnose some cases of rheumatoid arthritis as monosymptomatic or oligosymptomatic forms of systemic lupus erythematosus. To investigate this possibility two series of adult patients with rheumatoid arthritis were studied, and the test was also applied to several control series. The first of the two series consisted of 388 patients with rheumatoid arthritis. In order to exclude the unintentional selection of possible cases of lupus erythematosus, the second series comprised 100 unselected consecutive cases of rehumatoid arthritis as they were admitted to the department of rheumatology, University Hospital, Leyden, Netherlands. L. E. cells were found in 17% of the 488 patients with rheumatoid arthritis. This observation led to a statistical analysis of its clinical implications The group with the L. E.-cell phenomenon showed a higher frequency of splenomegaly, diseases of the lower respiratory tract, abnormal urinary sediment, anemia, false-positive tests for syphilis, and a high erythrocyte sedimentation rate that failed to fall after a first course of gold treatment. In individual patients with rheumatoid arthritis the positive L. E.-cell phenomenon was not related to a typical clinical picture.

The place of publication of the periodicals appears in brackets preceding each abstract.

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Familial Primary Systemic Amyloidosis: An Experimental Genetic and Clinical Study. J. G. Rukavina, W. D. Block and A. C. Curtis. J. Invest. Dermat. 27:111-131 (Sept.) 1956 [Baltimore].

The authors had an opportunity to study familial primary systemic amyloidosis when two cousins were referred to their hospital for the study of an unusual syndrome consisting essentially of neurological and ophthalmologic symptoms. Data obtained from these patients suggested a reservoir of clinically similar cases in a genetically isolated community. Sixty-six members of this pedigree agreed to be investigated for the presence or absence of clinical or subclinical inherited primary systemic amyloidosis by means of clinical, laboratory, and experimental biochemical methods. Approximately one-half of the 66 members of this family have been shown by clinical, laboratory, and experimental methods to be afflicted with clinical or subclinical primary systemic amyloidosis. In one patient clinical suspicion was confirmed at autopsy. In three others a positive tissue biopsy (skin and ovarian tissue) for amyloid deposition reenforced the presumptive diagnosis. Evidence secured by this study points to a dominant form of inheritance. More significantly it emphasizes the importance of the electrophoretic serum and lipoprotein relationship to the pathological process. The clinical signs and symptoms of familial amyloidosis described confirm the observations of previous investigators. In this family group, at least, the broad clinical spectrum represents a predictable, concatenated series of events culminating in order of descending frequency in peripheral neuropathy, skin changes, hepatic enlargement and dysfunction, cardiovascular insufficiency, eye changes, gastrointestinal symptoms, and splenomegaly. The occurrence of the carpal tunnel syndrome represents a previously unreported finding in the inherited form of the disease. In no case was there clinical evidence of macroglossia, bleeding tendency, or papulonodular dermatological manifestation of the disease.

The usual laboratory procedures were inadequate in the diagnosis of this process, but free electrophoresis of the serum of these patients revealed an atypical peak migrating between the beta and alpha-2 globulin areas, and ultracentrifugation demonstrated elevation of the serum lipoproteins. These methods should be used if primary systemic amyloidosis is to be recognized. The demonstration by ultracentrifugation of abnormally elevated lipoproteins, particularly in the -S 25-40 and 20-25 fractions, suggests that at least in part familial primary systemic amyloidosis represents an inherited aberration in lipoprotein metabolism.

Observations on Hepatic and Renal Dysfunction in Trichinosis: Anatomic Changes in These Organs Occurring in Cases of Trichinosis. J. M. Guattery, J. Milne and R. K. House. Am. J. Med. 21:567-582 (Oct.) 1956 [New York].

Functional and pathological derangements in the liver and kidney were observed in three men between the ages of 40 and 45 years and two women aged 18 and 23 years with trichinosis. Liver function tests were performed in the three men. Hepatic dysfunction was manifested by a reduction of bromsulfalein excretion in all; an abnormal result from this test was obtained 16 days after the onset of the initial symptoms in one of these patients. The men survived, but the two women died and autopsy was performed in both. Findings suggested that the hepatic changes may include direct invasion of the liver sinusoids by the Trichinella larvae; fatty changes and degeneration, particularly involving the peripheral zone of the liver lobule early in the course of the disease; and progression to frank cirrhosis.

Hypoalbuminemia was a prominent feature in four of the five patients. Maintaining the general nutrition of the patients was a major problem. All had pronounced anorexia; nausea, vomiting, and diarrhea were protracted in two. Malabsorption from the gastrointestinal tract may have been a factor. Nephritis occurred in three patients. Abnormal urinary findings consisted of albuminuria, hematuria, and granular and hyaline casts. Both glomerular and tubular damage was revealed by autopsy. Trichinosis may simulate acute and chronic glomerulonephritis.

Trichinosis in its severe form is a diffuse disease involving widespread vascular damage, widespread tissue invasion, and multiple organ damage. There is no specific therapy for trichinosis. A rigid program of care is important; this includes maintenance of adequate nutrition, alertness to possible intercurrent infections and to the possible diffuse nature of the disease, and provision of proper follow-up. Two of the severely ill patients received acetylsalicylic acid (aspirin) on a four-hour schedule with apparently satisfactory response. The use of salicylates will bear further investigation.

Diabetes Mellitus and Addison's Disease in Same Patient. V. Faber and P. Grønbaek. Ugesk. læger 118:985-988 (Aug. 23) 1956 (In Danish) [Copenhagen, Denmark].

To date 56 cases of simultaneous diabetes mellitus and Addison's disease have been reported. The combination occurred in all age groups, equally in men and women, with average duration of life of five years. In 38 cases diabetes mellitus developed on an average of eight years before the Addison's disease, in 13 cases Addison's disease preceded the diabetes by from one-half to five years, and in five cases the two diseases were diagnosed simultaneously. Because of the antagonistic action of the pancreas and the adrenal cortex on the carbohydrate metabolism, the combination of the two diseases presents diagnostic and therapeutic problems. While a falling insulin requirement in a diabetic patient should always suggest complicating Addison's disease, diabetes mellitus in an Addisonian patient will often be latent. With simultaneous onset of the two diseases, differential diagnosis of diabetic coma from an Addisonian crisis presents special difficulties. In the uncomplicated combination it is rational to treat the adrenal insufficiency first. Then, when the adrenal insufficiency is fully compensated, the diabetes is treated like an uncomplicated diabetes. In the case described, in a woman aged 29, the high blood sugar values and ketonuria testified for diabetic coma, but there was no Küssmaul respiration. Slightly lowered blood pressure and absence of diarrhea testified against Addison's disease, but the patient's marked insulin sensitivity pointed to adrenal insufficiency. The patient has been treated with desoxycorticosterone acetate, salt, diet, and insulin, and her condition has been satisfactory for a year and a half. She has not been given cortisone, as her diabetes was considerably aggravated following a cortisone test, with development of diabetic precoma. Cortisone treatment in the presence of both diseases seems to be rational only in the case of frequent and distressing hypoglycemic attacks.

Renal Vein Thrombosis and the Nephrotic Syndrome. V. E. Pollak, R. M. Kark, C. L. Pirani and others. Am. J. Med. 21:496-520 (Oct.) 1956 [New York].

Thrombosis of the renal vein with the nephrotic syndrome was observed in two men aged 29 and 35 years. The younger man died of massive gastrointestinal hemorrhage. The case of the patient who survived is described. He had multiple pulmonary infarctions and thrombosis of both common iliac veins. The nephrotic syndrome developed after gradual or incomplete occlusion of the left renal vein. Two months later more rapid occlusion of the right renal vein occurred. The right kidney became functionless and secondarily infected, and was removed. Treatment with anticoagulants and antibiotics reversed the previously relentless downhill course, and the patient thereafter made an uninterrupted recovery.

Fourteen cases of the clinical syndrome of thrombosis of the renal vein associated with the nephrotic syndrome in 9 male and 5 female patients between the ages of 12 and 72 years were collected from the literature. The clinical features varied with the rapidity of the onset and completeness of occlusion of the renal veins. Adults with thrombosis of the renal vein may have definite symptoms referable to the affected kidney, such as sudden onset of hematuria, lumbar pain and tenderness, and enlargement of the kidney. Often there is evidence of thromboembolism in the lungs, pelvis, extremities, and elsewhere. In others, all these symptoms may be of a milder degree or absent and the nephrotic syndrome of obscure origin may be the only clinical manifestation of the thrombosis of the renal vein. In between are patients with a combination of the nephrotic syndrome and evidence of thromboembolism.

Histological observations made on sections from serial percutaneous renal biopsies in the two patients and autopsy findings in these two patients and in five of those reported by other workers revealed that the glomerular basement membrane was thickened and the tubules were atrophied. The interstitial tissue was edematous at first and later became the seat of an extensive fibrosis. The changes in the tubules and interstices were out of proportion to those in the glomeruli.

SURGERY

Percutaneous Left Ventricular Puncture in the Assessment of Aortic Stenosis. R. Brock, B. B. Milstein and D. N. Ross. Thorax 11:163-171 (Sept.) 1956 [London, England].

Two questions have to be answered in assessing aortic valvular disease. The first is whether, in a patient with signs of pure aortic stenosis, symptoms such as angina or dyspnea are due to the aortic stenosis or to associated coronary or pulmonary disease. The second is whether aortic stenosis or regurgitation is dominant in a patient who has a mixed lesion. These questions cannot be answered by indirect methods of investigation. Measurement of the systolic pressure gradient across the aortic valve is a routine procedure at operation for aortic stenosis. The authors have now developed a method by which this information can be derived from preoperative left ventricular pressure measurements. They measure the gradient by direct puncture of the left ventricle through the intact chest wall and simultaneous brachial artery puncture. The procedure is simple and safe, causes no disturbance to the patient, and has given rise to no serious complications. It has now been performed 24 times.

The technique is simple, and in most cases the apex of the left ventricle seems to be almost subcutaneous. The ease with which the left ventricular pressure is obtained contrasts strongly with other less direct methods. Moreover, as a large needle can be used, a pure undamped tracing much superior to that obtained through a long fine catheter is recorded. This makes analysis of the record simple and more accurate. The authors never failed to enter the left ventricle in any case. In one patient who had cor pulmonale as well as aortic stenosis with a very large right ventricle extending electrocardiographically as far as V6, the needle inserted at the apex entered the right ventricle and a second puncture further back was necessary to enter the left ventricle. In 10 of these patients the needle was advanced as far as possible up the outflow tract and it was found that it could be advanced for a further 10 cm. after the ventricle was first entered before extrasystoles appeared on the electrocardiograph, suggesting that the needle had again penetrated the myocardium. Thus it seems that if the needle is passed along the line of the outflow tract it will remain in the ventricular cavity. The procedure is no more disturbing to the patient than the brachial artery puncture and far less so than puncture of the left atrium from the posterior chest wall.

Indications for Lobectomy in the Treatment of Carcinoma of the Lung. J. L. Robinson, J. C. Jones and B. W. Meyer. J. Thoracic Surg. 32:500-507 (Oct.) 1956 [St. Louis].

The 79 resections carried out by the authors for pulmonary carcinoma up to 1950 included only 3 lobectomies, but later, when as the result of a chest x-ray survey many patients with small, round, circumscribed, peripheral lesions came to surgery, they made wider use of lobectomies. Whereas before 1950 the proportion of lobectomies had been 3.8% of pulmonary resections, it jumped to 30.4% in 1950, and for the past two years the number of lobectomies has exceeded the number of pneumonectomies. Follow-up revealed that the three-year survival was 16.3% in 123 patients treated by pneumonectomy but 71.4% in 21 patients treated by lobectomy.

The authors made a survey among the surgeon members of the American Association for Thoracic Surgery to determine to what extent and under what conditions they are using lobectomy in treating patients with carcinoma of the lung. The results of that survey show that, of 318 surgeons replying, 91.8% use lobectomy in treating metastatic pulmonary carcinoma and 92.8% use lobectomy in treating primary pulmonary carcinoma. About 60% use it as an operation of choice in treating primary carcinoma of the lung; 40% use it only in patients whom they feel would not tolerate a pneumonectomy. Of the 318 surgeons who replied, 227 believe that they have sufficient experience with lobectomy to be able to offer an unqualified opinion regarding its efficacy. Seventy-six per cent (56.9% of the total replying) believe it offers as good a chance for long-term survival as does pneumonectomy, and only 24% (17.8% of the total) do not. On the basis of the replies to the questionnaires, as well as their own experience, the authors suggest the following points as a guide for lobectomy in pulmonary carcinoma. 1. It is the operation of choice in a peripheral lesion located well away from the fissures or adjacent lobes, with a satisfactory proximal length of uninvolved bronchus, and with no apparent extension to adjacent tissues or to the peribronchial, hilar, or mediastinal lymph nodes 2. It is a compromise operation in patients whose lesions do not satisfy the above conditions but whose cardiorespiratory or other clinical condition makes them unsatisfactory subjects for total pneumonectomy. 3. It is a palliative operation in patients who, at the time of operation, are found to have a lesion that obviously cannot be completely eradicated surgically but in whom such symptoms as hemoptysis, cough, or infection can be controlled better by lobectomy than by nonsurgical means.

Pneumonectomy for Pulmonary Tuberculosis: An Analysis of 151 Cases. V. O. Björk. J. Thoracic Surg. 32:528-547 (Oct.) 1956 [St. Louis].

Björk discusses the pathophysiological problems arising in the surgical treatment of 151 bad-risk patients undergoing pneumonectomy for pulmonary tuberculosis. Many patients undergoing this operation are in bad condition. They may have toxic conditions, having had fever, with considerable expectoration, for several months. The respiratory reserve is usually small owing either to disease of the only functioning lung or residues of a previous pneumothorax. One hundred eleven of the 151 patients have been followed for from one to five years or more, of the other 40 patients 16 are dead, 22 were observed for less than a year, and 2 could not be traced.

Pneumonectomy is reserved for destroyed lungs whether bronchial stenosis is present or not. A one-stage procedure with resection and osteoplastic wall thoracoplasty is recommended If the function of the remaining lung is impaired by disease or an old pneumothorax, the respiratory work for the patient in the postoperative period is often too great, with carbon dioxide retention as the result. Under these conditions prolonged artificial ventilation through a tracheostomy is indicated until the patient has regained strength enough to perform adequate ventilation and bring up the secretion. Of 111 patients followed one to five years after operation, 97, or 87%, are considered cured. Of the 11 patients with recurrence, 5 are well and working, with negative sputum but with a postive guinea pig test in the gastric washings

The Surgical Treatment of Pulmonary Tuberculosis in Childhood and Adolescence. D. W. Huish. Thorax 11:186-200 (Sept.) 1956 [London, England].

Huish reviews observations on 29 children under the age of 16 years who were subjected to major surgical procedures in the treatment of pulmonary tuberculosis. The children were resident in the eastern part of central Scotland, coming from both urban and rural areas. They derive from a population of some 500,000 people. Fifteen children were operated on for primary lesions, 14 for chronic "adult type" lesions. The 15 children with primary tuberculosis included 9 with segmented or lobar lesions, on whom 10 operations were performed, including 8 lobectomies There were two surgical, but no late, deaths. Lobectomies were performed also in two children in whom segmental or lobar lesions had caused bronchiectasis. Primary cavitation was established in only one patient, a 3-year-old girl, who obtained an excellent result from lobectomy. Thoracotomy with the intention of decorticating the left lung was carried out in a 12-year-old boy. The operation had to be abandoned, and medical treatment was resumed. Chronic fibroid lung resulted in 2 of the 15 patients with primary lesions. A whole lung was involved in both patients resulting in fibrous contraction of the lung with bronchiectasis One was cured by pneumonectomy. Decortication was attempted but had to be abandoned in the second patient with fibroid lung.

Of the 14 children who were operated on for chronic pulmonary tuberculosis, five had lesions that arose in close clinical relation to a primary infection and the other 9 showed the type of disease usually seen in young adults. The clinical course in all of them indicated a severe form of tuberculosis. Fourteen operations were performed: lobectomy in 7, extrapleural pneumolysis in 6, and open intrapleural pneumolysis in one. The one operative death in this group resulted from massive collapse of the other lung. The author concludes that surgery has a place in the treatment of primary pulmonary tuberculosis in childhood. Up to the present it has been employed mainly for the removal of irretrievably damaged lung tissue, but with the aid of more accurate pathological diagnosis there is a prospect of employing surgery to prevent such damage. The indications for surgical treatment of chronic pulmonary tuberculosis in children and adolescents are much the same as in adults, but collapse operations have little place, and in this age group resection is the method of choice.

Postgastrectomy Syndrome. H. K. Lassen. Ugesk. læger 118:1005-1012 (Aug. 30) 1956 (In Danish) [Copenhagen, Denmark].

From 1948 to 1953 subtotal gastrectomy for gastric or duodenal ulcer was carried out in 221 patients in Central Hospital in Randers. Follow-up of 163 of the 165 survivors (147 men, 16 women, aged mostly between 40 and 60) showed good results in 86, or 52.8%, satisfactory results with slight symptoms in 61, or 37.4%, and poor results in 16, or 9.8%. The dumping syndrome occurred in 36%, loss of weight was fairly frequent, anemia was seen in only 5 out of 137 patients, and active pulmonary tuberculosis had developed in two. There is no satisfactory explanation as to why certain persons have symptoms after resection for ulcer and others, fortunately the majority, have no special distress. The resection should not be too large, if it can be avoided, in order not to cause difficulty because of the small gastric stump, nor should it be too small because of the risk of occurrence of marginal or jejunal ulcer. Resection is the best treatment available for ulcer symptoms of longer duration. The dumping syndrome may be referable partly to purely mechanical causes, partly to an abnormal blood sugar curve with early hyperglycemia and late hypoglycemia, and partly to a shock-like condition with reduction in plasma volume. Possible loss of weight is due partly to the patient's asthenic type, partly to the presence of dumping or anorexia. The anemia, of a sideropenic kind, is due to reduced iron absorption. Other sequels are relatively rare.

Treatment of Diabetes Mellitus in Surgical Complications: Review and Suggestion. J. Pedersen. Ugesk. læger 118:971-979 (Aug. 23) 1956 (In Danish) [Copenhagen, Denmark].

A patient whose diabetes has been regulated for about three weeks with intensive diabetic preoperative treatment tolerates an ordinary operation without losing his regulation. The number of diabetic persons with surgical diseases is increasing and at the same time the relative frequency of these diseases is shifting, with diseases such as cancer increasing more than gangrene or infection. The decisive factor in treatment is the late diabetic complications, and most of the patients will have cardiovascular disorders. A number of patients have diabetes without glycosuria (high renal threshold). The author stresses the importance of preoperative prophylactic treatment aiming at a normal daily blood sugar level. A diabetic patient should not be treated operatively without the participation of an internist experienced in diabetes. The cooperation of surgeon, anesthesiologist, and internist should be routine. The importance of the personal factor is especially emphasized, i. e., that the treatment should be conducted by only a few persons and that in large hospitals with several surgical departments the treatment should be centralized.

Below-Knee Amputation in Arteriosclerotic Gangrene. R. R. Kendrick. Brit. J. Surg. 43:13-17 (July) 1956 [Bristol, England].

Kendrick has for several years employed below-the-knee amputations in preference to the above-the-knee amputations whenever possible. In a consecutive series of 59 amputations of the lower limb for obliterative arterial disease, 51 were performed through the calf, and of these 32 (63%) healed by first intention. Three patients died. Healing failed in two cases, and above-knee amputation was required. In addition, massive necrosis occurred in one stump, which had remained soundly healed for 18 months. Refrigeration anesthesia is of value in a few patients in whom the operative risk is very great. The formation of a hematoma is a serious complication in these amputations, and, unless the wound is completely dry, drainage is preferred.

Amputation below the knee permits better balance either with crutches or with a prosthesis; this difference in the elderly patient may mean that he is ambulatory. Walking is achieved following a below-knee amputation with greater facility and far less physical effort because of the longer and more efficient lever present. The below-knee stump is rarely associated with stump or phantom limb pains; also, of course, the desirable normal movements of the knee-joint are retained. The patient with a below-knee amputation has greater stability and freedom of movement when seated in a chair or even lying in bed, and it must be remembered that not infrequently both legs will eventually require amputation.

Acute Appendicitis in Infancy and Childhood: A Critical Review of Seven Years' Experience in a Children's Hospital. C. W. McLaughlin Jr. and C. Organ. Am. J. Surg. 92:558-561 (Oct.) 1956 [New York].

The authors analyze a consecutive series of 300 infants and children coming to surgery with the diagnosis of acute appendicitis. Twelve per cent of the patients in this series were admitted with perforated appendixes and 3.2% with appendiceal abscesses. The 300 children were operated on by the attending surgical staff of the Children's Memorial Hospital in Omaha. A McBurney incision was employed in 60%, a transverse incision in 17%, a right rectus incision in 15%, and a Davis or paramedian incision in 8%. The appendiceal stump was simply ligated in 87% and inverted after ligation in 13%. Closure with drains into the peritoneal cavity was used in 58% of the children with perforation but without definite abscess; in the other children with perforation and without abscess tight closure was used without serious complication. The 10 children with appendiceal abscesses had been ill an average of six and a half days on admission, and the conditions of some were extremely toxic. After suitable preparation with fluids, blood if indicated, and antibiotics, 8 of these 10 patients were operated on. In three of the eight only drainage of the appendiceal abscess was accomplished, with subsequent appendectomy three months later. In five of the eight primary appendectomy was carried out with drainage of the abscess. Two patients were handled conservatively with resolution of the abscess and the recommendation that appendectomy be performed subsequently. There were no deaths in the entire series of 300. Acute appendicitis in infancy and childhood, while still potentially a very serious disease, is rapidly becoming one of those that are well understood. Therapy is becoming standardized, and results are approaching the ideal.

NEUROLOGY & PSYCHIATRY

Benign Cysts of the Brain Simulating Brain Tumor. H. Handa and P. C. Bucy. J. Neurosurg. 13:489-499 (Sept.) 1956 [Springfield, Ill.].

The term "benign cyst of the brain" generally indicates either a porencephalic or an arachnoidal cyst. Any symptoms of cerebral involvement presented by patients with porencephalic cysts arise as the result of the cerebral defect and not because of the cyst, which is a purely passive and secondary development. The symptoms most commonly seen in such cases are hemiparesis and convulsions. Arachnoidal cysts may arise secondary to an infectious or inflammatory process in the leptomeninx, or they may be congenital or occur following severe cerebral trauma. If symptoms of cerebral involvement are present with such cysts, convulsions are the most common. The three patients whose histories are reported had brain cysts that did not fall into either of these categories, nor were they of neoplastic origin. These cysts lay within the brain substance and did not communicate either with the ventricular system or the subarachnoid space. Two of these cysts lay in the cerebral hemisphere and one was in the cerebellum. All three patients presented themselves with serious signs and symptoms of an intracranial space-occupying lesion with signs of increased intracranial pressure and of focal lesions of the brain. All three cysts were treated surgically. One was simply aspirated on several occasions. One of the others was opened into the lateral ventricle, while the posterior wall of the cerebellar cyst was removed so that it communicated with the cisterna magna. All three patients recovered and have been well for many years.

Encephalitis with Papilledema: Picture Causing Suspicion of Intracranial Tumor: Preliminary Report. J. H. Rasmussen. Ugesk. læger 118:955-957 (Aug. 16) (In Danish) [Copenhagen, Denmark].

Sixty-two patients admitted to the neurological department of Aarhus General Hospital in the three-year period beginning in 1952 presented a picture suggesting intracranial tumor. The symptoms were usually vague and had lasted for from a few weeks to a few months. Objective examination showed papilledema, in some cases also focal deficiency. Carotid angiography gave negative results. Ventriculography in 57 cases disclosed no signs of a localized, space-filling process. No evidence of intracranial tumor was found in the six patients operated on. The course of the disease was prolonged, but most of the patients were able to return to work before the papilledema disappeared. The long-range prognosis is favorable. Five patients died, 46 are well, 2 are well except for a visual defect, and in one the course is greatly protracted; in eight patients no satisfactory follow-up examination has yet been made. It is believed that in most cases there was an encephalitis with brain edema also affecting the papilla of the optic nerve as the main feature. The assumption is supported by the fact that there was an uncharacteristic febrile period in several of the patients.

Chronic Hypoventilation in an Epileptic Patient. C. E. Wells. Neurology 6:744-749 (Oct.) 1956 [Minneapolis].

Wells reports the case of a 19-year-old man in whom seizures had begun at 7 years of age. The seizures consisted of brief episodes of loss of contact with his environment, with staring or blinking of the eyelids, sometimes accompanied by head nodding and bilaterally symmetric jerks of the upper extremities. At the age of 14 he began to have rare generalized convulsions, characterized by prolonged loss of consciousness, clonic movements of all extremities, chewing motions of the mouth, and tongue biting. The patient was of normal intelligence, and no significant abnormalities were found on neurological or on general physical examination. In the course of electroencephalographic studies it was found that during periods of hyperventilation the electroencephalogram showed evidence of markedly increased activity and frequently showed paroxysmal bursts of epileptiform activity lasting 90% or more of the hyperpneic testing period. Blood electrolytes showed his venous serum carbon dioxide content to be above the range of normal. The patient was given Diamox in an attempt to alleviate the seizures, but the frequency of seizures remained uninfluenced. Although the total carbon dioxide content fell during Diamox therapy, there was no significant change in dissolved carbon dioxide as carbonic acid or in carbon dioxide tension. The author cites reports on the clinical usefulness of hyperpnea as a diagnostic method in epilepsy. Efforts have been made to prevent epileptic seizures by inducing chronic hypoventilation by means of bilateral artificial pneumothorax.

Surgical Treatment of Arteriosclerotic Occlusion of Common Carotid Artery. D. A. Cooley, Y. D. Al-Naaman and C. A. Carton. J. Neurosurg. 13:500-506 (Sept.) 1956 [Springfield, Ill.].

This report is concerned with a 71-year-old man who complained of a swishing noise in his left ear. The noise had first appeared four months previously and had steadily increased in intensity. It was synchronous with heart beat and was most annoying during periods of accelerated heart rate. The noise was accentuated by slight flexion of the head on the neck, particularly if his head was on a pillow, thus interfering with sleep. Cerebral arteriography showed a partial occlusion of the left common carotid artery beginning just proximal to the bifurcation, with satisfactory filling of the internal and external divisions. Localized aneurysmal dilatation of the internal carotid artery was demonstrated distal to the stenosis. At operation, thromboendarterectomy was performed, reconstructing the artery while a temporary external shunt was used to provide cerebral circulation. The patient was discharged from the hospital six days after operation with slight impairment of motion and sensation in the right hand. Four weeks later examination revealed normal pulsation in the left common and external carotid arteries without evidence of a thrill or bruit. The slight residual weakness in the right hand was improving, and function was almost normal.

Although this patient had no neurological deficit before operation, the results of the carotid occlusion test indicated that cerebral circulation was precariously reduced. Under such circumstances even slight reduction in cardiac output or periods of hypotension from any cause may produce temporary hemiplegia from ischemia even in the absence of complete carotid occlusion. Furthermore, the narrow lumen of the carotid artery could easily have been occluded acutely by development of a very small thrombus. If operation had been postponed until permanent damage to cerebral tissue had occurred, little could have been expected from the restoration of normal carotid circulation. The authors emphasize the fact that arteriosclerotic occlusion of the common or internal carotid arteries is not uncommon and may produce neurological symptoms of varying types and severity. Onset may be explosive in character, producing hemiplegia, or insidious, producing slowly progressive or transient symptoms. Prompt recognition of the disease and localization of the occlusive lesion permits early treatment and may prevent permanent neurological symptoms.

A Particular Variety of Headache. C. Symonds. Brain 79:217-232 (June) 1956 [London, England].

The author defines a clinical syndrome that is of comparatively rare occurrence but is recognized by many neurologists. The 17 patients discussed in this report were selected from a larger number. Attacks of severe pain in and around the eye occurred in bouts, with long intervals of freedom. The duration of the attack or paroxysm was seldom less than half an hour or more than two hours. The frequency of the paroxysms during a bout varied from less than one to eight in 24 hours. The duration of the bout was usually between two and eight weeks. The intervals of freedom lasted in most cases for more than six months and extended up to 10 years. Fourteen of the patients were males, and the average age at onset was 27. The successful treatment of this malady by preventive injections of ergotamine tartrate is described with illustrative cases.

The author believes that this particular variety of headache is a migrainous variant. The justification for regarding this variety of headache as a distinct clinical species is that, since the bouts are self-limited and seldom last more than 8 or 10 weeks, they can be treated by repeated injections of ergotamine tartrate without any harmful effects of a lasting nature. It was observed that ergotamine tartrate in solution is unstable, so that the preparation after a period of months may become inert. A patient who has previously obtained relief from the injections and who after an interval of freedom has another bout may, having recourse to an unused store of ampuls, find them ineffective. This has occurred in more than one case of the present series, the subsequent use of fresh ampuls being followed by immediate relief.

PEDIATRICS

Hormone Therapy Combined with Antibiotics in the Treatment of Tuberculous Meningitis in Children. J. Chaptal, R. Jean, Mrs. C. Campo and Mrs. D. Abram-Dossa. Pédiatrie 11:663-675 (No. 6) 1956 (In French) [Lyon, France].

Cortisone was given simultaneously with streptomycin and isoniazid in 15 cases of severe tuberculous meningitis in children whose ages ranged from 5 months to 11 years. The purpose of the cortisone was to avoid the rise in intracranial pressure and the general exacerbation of symptoms that are commonly seen during the first few weeks of antibiotic therapy in cases far advanced or not promptly diagnosed. The adverse effects of the antibiotics are ascribed to liberation of toxins from the tubercle bacilli as they undergo lysis; there may be an arachnoiditis about the cord and the base of the brain, manifested by increased albumin in the spinal fluid and leading to permanent, possibly fatal, nervous lesions. The initial exacerbation caused by antibiotics was clearly seen in three infants with the syndrome of intracranial hypertension: daily systemic administration of 50 to 100 mg. of hydrocortisone was followed by distinct improvement within a few days. In subsequent cases it was found that daily oral administration of cortisone, if begun simultaneously with the beginning of antibiotic therapy, suppressed the initial stage of aggravation, so that improvement was obtained within three to eight days. Administration of the cortisone by lumbar puncture did not benefit patients with arachnoiditis about the base of the brain but was strikingly successful in one case of spinal arachnoiditis, where the anti-inflammatory effect of the hormone was enhanced by proximity of the site of injection to the structures actually involved. The systemic route of administration is generally preferable to the intraspinal route, and hormone therapy should begin simultaneously with antibiotic therapy. If prolonged hormone therapy is necessary, the adrenocorticotropic hormone ACTH may be given alternately with cortisone. The cases here described indicate that simultaneous hormone and antibiotic therapy in tuberculous meningitis is not merely a possibility but actually, because of the great bactericidal potency of the antibiotics, a necessity.

Cystic Fibrosis of the Pancreas with Varying Degrees of Pancreatic Insufficiency. H. Shwachman, R. R. Dooley, F. Guilmette and others. A. M. A. J. Dis. Child. 92:347-368 (Oct.) 1956 [Chicago].

Seventeen children, between the ages of 2 months and 16 years when first seen, with cystic fibrosis of the pancreas were studied at the Children's Medical Center of the Harvard Medical School between July, 1947, and March, 1956. Partial or incomplete pancreatic insufficiency was a feature in all the patients; in each of them the duodenal fluid, when first examined, showed normal or near-normal proteolytic activity. The pulmonary manifestations of the disease preceded and overshadowed the symptoms and laboratory evidence of pancreatic insufficiency. Four of the patients died of extensive pulmonary infection and insufficiency, and autopsy showed marked fibrosis of the pancreas with some inspissated secretion in a number of widely dilated ducts and with preservation of acinar tissue. Six of the 14 patients who survived were followed for a sufficiently long period by repeated duodenal fluid assays to demonstrate progression from a state of partial to one of complete pancreatic enzyme deficiency. Dissociation of or lack of correlation of the activity of the various pancreatic enzymes in the duodenal aspirate was frequently noted in these patients.

The diagnosis of cystic fibrosis was made in all the patients before complete enzyme deficiency occurred. The features that led to this diagnosis in patients who had only the pulmonary features of cystic fibrosis were positive family history, abnormally increased viscosity of duodenal fluid, scant flow, dissociation of enzyme activity, failure of normal enzyme response to intraduodenal instillation of olive oil serving as a pancreatic stimulus, loss of enzyme activity in successive tests over a period of months or years, and abnormal results obtained from gelatin and vitamin A–absorption tests. When the sweat test was made simple, reliable, and practical, the patients in whom a diagnosis of partial pancreatic insufficiency had been made were recalled for study. In each of 15 patients tested the findings for the sweat sodium and chloride concentration were characteristic of patients with cystic fibrosis having complete pancreatic deficiency. It has been estimated that from 10 to 15% of 500 patients with cystic fibrosis studied during the past nine years had minimal or no discernible evidence of pancreatic enzyme deficiency.

The observations made in the 17 patients are opposed to a hypothesis for this disease, that places the initial or primary defect in the pancreas. Pulmonary lesions may appear long before pancreatic enzyme deficiency can be detected by current laboratory tests or by clinical observation. The severity and extent of the pulmonary lesion is independent of the status of the pancreas. Caution is suggested in the use of a trypsin assay of the duodenal fluid as a reflection of pancreatic function. The marked fluctuation in activity of this organ and the wide normal range of activity of some individual components must be considered in evaluating the pancreatic status. A number of tests reflecting different functions of the pancreas, such as the so-called direct tests including measurements of protease, amylase, lipase activity and the response to intravenous administration of secretin or intraduodenal instillation of olive oil, and indirect tests including absorption tests (fats, vitamin A, and proteins), may provide a truer index of the status of the pancreas. The prognosis in cystic fibrosis does not depend on pancreatic insufficiency but rather on the pulmonary involvement. The recognition of cystic fibrosis in patients with varying degrees of pancreatic involvement permits the institution of therapy directed toward the pulmonary infection and mechanical obstructive phenomena. It was this approach that accounted for the survival of most of the patients with extensive pulmonary involvement reported on.

Migraine in Childhood: A Preliminary Report. E. C. Burke and G. A Peters. A. M. A. J. Dis. Child. 92:330-336 (Oct.) 1956 [Chicago].

A diagnosis of migraine was made in 92 of about 60,000 children who were examined in the section of pediatrics at the Mayo Clinic in the course of a six-year period. There were 63 boys and 29 girls, and their age varied between 1½ and 14 years. Positive histories of migraine in members of the immediate family and grandparents were obtained in 40 children. Frontal or orbital headaches were described by 63 children, and in 13 others the headaches were unilateral or occipital. The most distressing symptoms were nausea and vomiting, which were present in 74 children. Only nine children described symptoms of scotoma, and nine others complained of blurred vision. Coexisting convulsive disorders were present in 7 of 18 children who had associated neurological features, such as numbness in the arms or hands, hemiplegia, expressive aphasia, amnesia, homonymous hemianopsia, and a hissing sound in the ears. A strikingly high incidence of abnormal tracings was noted in 46 of 67 children from whom electroencephalograms were obtained. Twenty-two children had manifested vascular changes about the temple or face. These were described at various times as a flushing of the face or temple, an ashen-gray pallor, or bloodshot eyes. The frequency of occurrence of migrainous attacks ranged from attacks nearly every day to one every month. In 26 children attacks of migraine were definitely associated with such precipitating factors as excitement, school examinations, family strife, a new dress, a trip to the barbershop, or other emotional factors. Physical exertion and fatigue, television, movies, or bright sunshine were also precipitating factors.

Migraine occurs oftener in children than is appreciated. Children with migraine have scotoma less frequently than do adults with migraine. They also have less cephalgia, but more gastrointestinal symptoms, than do similarly afflicted adults. The migrainous child has attacks more frequently than does the adult with migraine. Boys were more frequently affected than girls. Migraine is a vascular phenomenon of unknown cause. Psychogenic factors appear to play the greatest role in precipitating attacks. Elimination of these factors and an understanding of the mechanism of the attacks are essential for both patient and parents. The study of migraine is complicated because of numerous functional aspects in the headaches of these children as a group.

The prognosis for disappearance of attacks cannot be given with statistical proof at this time. Additional studies concerning this aspect of the problem are indicated. The authors recommend administration of acetylsalicylic acid (Aspirin), a combination of ergotamine tartrate and caffeine (Cafergot), and the use of diphenylhydantoin sodium (Dilantin). A trial of anticonvulsant drugs in adequate doses is suggested as a prophylactic measure.

"Periodic Peritonitis." G. S. Sturtz and E. C. Burke. A. M. A. J. Dis. Child. 92:390-394 (Oct.) 1956 [Chicago].

The authors describe three cases of periodic peritonitis in a 6-year-old boy of Armenian extraction, an 11-year-old boy of Syrian extraction, and an 11-year-old Jewish girl. Periodic peritonitis is characterized by recurrent bouts of abdominal pain, abdominal tenderness, fever, polymorphonuclear leukocytosis, and at times, pain in the thorax and joints. The duration of the attacks may vary from 24 to 72 hours; it is followed by complete remission, but exacerbations occur at regular intervals. The recurrences at times may be irregular, and the remissions may become shorter with age. The three cases appear to be the first reported in the American pediatric literature, but the syndrome is familiar to internists in the United States and to physicians in the Near East and North Africa. It often occurs in families. In most reported cases the disease has afflicted Armenians, Jews, and Arabs. The paroxysms recur over many years and are unaffected by any treatment. There is no appreciable effect on the general health or growth or development of afflicted children. The cause of this syndrome is unknown.

The younger of the two boys had an exploratory laparotomy between attacks. His abdominal organs and peritoneum were grossly normal. The older boy who was operated on during an attack of abdominal pain and fever had peritonitis grossly. The reaction was severest around the spleen and gallbladder. It appears that patients operated on during an attack often have acute peritonitis and sometimes superimposed chronic peritonitis, while those who are operated on during remission may have chronic peritonitis or no peritoneal abnormality at all. Knowledge of this syndrome may allow the physician to recognize the fact that a patient has an attack. Exploratory laparotomy, however, may be necessary in some cases, if localizing signs develop, to rule out concomitant acute surgical disease.

OPHTHALMOLOGY

Retinopathy in the Premature. G. P. Sourdille, M. Pasquier and J. R. Grislain. Semaine hôp. Paris 32:2771-2778 (Sept. 10-14) 1956 (In French) [Paris, France].

Retinal disease of the newborn, unknown at Nantes before the creation there of the premature center in 1951, appeared in 56 infants during the four-and-a-half-year period from March, 1951, to October, 1955. Complete retrolental fibroplasia developed in 13, partial fibroplasia in 5, and regressive retinal disease that disappeared without sequelae in 38. The 13 infants with complete retrolental fibroplasia constituted 2.2% of all 600 premature infants examined and discharged alive during the period in question, but when only the 330 infants weighing less than 2,000 gm. are considered, the percentage is 4.3.

The variable effect of the disease on ocular function, ranging from normal vision to complete blindness, has led to attempts to determine the prognostic significance of the ophthalmoscopic findings. Rapidity of development, vitreous disturbances, vascularization of the iris, and tight miosis responding poorly to atropine seem to be unfavorable findings, but none is certainly so, and all must be interpreted in connection with the infant's birth weight and any possible toxic or infectious complications. Severe retinal disease in 17 infants was associated with a toxic syndrome and serious diarrhea in 7 and with severe persistent jaundice in 4. By contrast, only two cases of complete retrolental fibroplasia and three that were partial occurred in infants weighing 1,000 to 1,500 gm. whose hospital stay was uncomplicated by toxic or infectious incidents. Toxicity and infection undoubtedly predispose premature infants to retinal disease and aggravate the retrolental lesions when they occur.

The only effective treatment is preventive. The use of oxygen, which is unquestionably injurious to the retina of the premature infant, should be reduced to the minimum. A policy of giving oxygen in small amounts for short periods only was adopted at the premature center in October, 1954, and since then not a single case of complete or partial retrolental fibroplasia has been seen, and even the regressive forms have disappeared.

Factitious Improvement in Vision: Studies in the Pathological Physiology of the Arterioles and Capillaries. Jean-Gallois. Presse méd. 64:1528-1530 (Sept. 22) 1956 (In French) [Paris, France].

Patients with objectively demonstrated impairment of eyesight have been observed repeatedly to manifest functional improvement after the administration of vasodilating drugs without any corresponding improvement in the underlying disease of the eye. The functional improvement, though generally transient, has in some cases been long lasting. Three instances are briefly noted here. One patient had chorioretinitis; the second, amblyopia without visible lesion; the third, vascular changes in the retina. All received nicotinic acid; the third received, in addition, glutamic acid and a collyrium containing 1% potassium iodide. In each, the functional improvement was definite and prolonged.

Differential Diagnosis of Hysteria and Malingering in Functional Amblyopia: Report of a Case. H. A. Lincoff and J. Ennis. Am. J. Ophth. 42:415-421 (Sept.) 1956 [Chicago].

A diagnosis of functional blindness is the most that can be obtained by the various visual tests. For the further differentiation between the hysteric and the malingerer, other factors must be considered. In the case presented, visual testing established the presence of functional amblyopia in a young boy. The patient then admitted that he had profited from his disability, which would seem to indicate that he was a malingerer. Further examination revealed, however, that the basic disorder was hysterical. The differential diagnosis of hysteria and malingering is theoretically clear-cut. It is the difference between simulation in malingering and unconscious determination in hysteria. In practice, however, the delineation is not always so sharply and easily made, since there are varying degrees of awareness of the secondary gains in hysteria. The two conditions are most readily confused by those who mistakenly consider all hysterics as malingerers who can volitionally control their symptoms. Discrepancies, contradictions, and bizarre exaggerations of symptoms, are suggestive of malingering. The absence of much anxiety about symptoms, as in the reported case, is indicative of hysteria. The reoccurrence of anxiety following the cure of the visual defect further indicates the defensive nature of the symptom and reinforces the impression of hysteria, as does the patient's extreme suggestibility, indicated by his initial iatrogenic and later therapeutic responsiveness. Finally, data from the history and psychological testing revealed evidence of much repression of anxiety-provoking impulses, a finding always present in hysteria.

The Scleral Insert (Sclerocleisis) for Glaucoma: A Preliminary Report of Three Cases. A. B. Vicencio. Am. J. Ophth. 42:402-405 (Sept.) 1956 [Chicago].

The scleral insert or "sclerocleisis" follows the principle of iridencleisis and is similar to the techniques employing inserts and setons by which a filtering channel is obtained between the anterior chamber and the subconjunctival space. A limbus-based conjunctival flap is incised, dissected, and folded over the cornea below, as for iridencleisis. A half-thickness lamellar scleral strip about 3 mm. wide and 6 mm. long (giving allowance for shrinkage) is dissected by a no. 15 Bard-Parker knife from above downward, the base of the scleral flap being attached to the limbus. Just anterior to the base of the strip of sclera (1 to 2 mm. is the best) a keratome incision is made at the limbus, 3 to 4 mm. long, and into the anterior chamber. With fine forceps, the very soft and pliable scleral strip is easily inserted between the sclerocorneal incision into the anterior chamber. The conjunctival flap is closed with continuous silk sutures. The basic difference between iridencleisis and sclerocleisis is that, in the former procedure, the iris is pulled out of the anterior chamber and, in the latter, the scleral strip is pushed into the anterior chamber. The author presents the histories of three glaucoma patients in whom sclerocleisis was performed. The results appear to be promising.

INDUSTRIAL MEDICINE

Pneumonoconiosis Due to Inhalation of Abrasive Powder by Anergic Person: BCG Vaccination. R. E. Vaccarezza, F. A. Dubra and C. Urtubey. Rev. Asoc. méd. argent. 70:189-192 (July 15-30) 1956 (In Spanish) [Buenos Aires, Argentina].

A woman 20 years old started to work in a factory turning out abrasive soap. At the end of 3½ years she began to complain of backache, weakness, and loss of weight. She had no contact with tuberculous patients. Roentgen examination of the chest showed pure pneumonoconiosis of a confluent nodular type. The erythrocyte sedimentation rate was accelerated. Work was immediately discontinued. The severity of the pneumonoconiotic lesions was in contrast with the lack of clinical symptoms and respiratory difficulty. Repeated tuberculin tests and investigation of the gastric contents for tubercle bacilli gave negative results. The results of BCG vaccination were negative for 35 days, after which the vaccinal nodule appeared and tuberculin allergy became evident. The treatment consisted of rest and of administration of vitamins and liver extract injections. Serial roentgenograms taken during the four-year follow-up period showed massive fibrosis of a pure pneumonoconiotic type that progressed slowly. An attenuated tuberculin reaction persists. Pure pneumonoconiosis of a massive fibrous type may develop in the absence of pulmonary tuberculosis. The progress of the pulmonary lesions continues even if the patient no longer breathes an atmosphere laden with quartz. Pulmonary tuberculosis does not predispose to pneumonoconiosis, but pneumonoconiosis predisposes to pulmonary tuberculosis. Pneumonoconiosis, as a complication of pulmonary tuberculosis, aggravates the pulmonary tuberculous lesions. BCG vaccination does not change pure pneumonoconiotic lesions into pulmonary tuberculosis with pneumonoconiosis. The sedimentation rate of the erythrocytes can be accelerated in either or both pure pneumonoconiosis and pneumonoconiosis with pulmonary tuberculosis. Therefore, it cannot be used in the differential diagnosis of these two forms of pneumonoconiosis. Measures for industrial prevention of pneumonoconiosis include the following: (1) BCG vaccination of anergic applicants for work in industries dealing with quartz (the vaccination should be given several months before the applicant starts work), (2) treatment of pulmonary tuberculosis for workers in whom primary infection is detected, and (3) nonemployment of persons with grave sequels of pulmonary tuberculosis in industries in which quartz is handled.

Trichloroethylene Poisoning. H. B. Stentiford and C. J. H. Logan. Lancet 2:659-660 (Sept. 29) 1956 [London, England].

A 22-year-old man was in deep coma when hospitalized. About 1½ hours before he had drunk some cleaning fluid obtained from a clothing factory where he had been employed. It was later estimated that he probably ingested nearly 5 oz. of trichloroethylene. He behaved normally for a minute or two, but then stood up, staggered across the room, fell to the floor, and became unconscious. His breath smelled strongly of trichloroethylene. He was pale and sweating, and his jaws were tightly clenched. There was no response to painful stimuli, his limbs were flaccid, and his tendon reflexes were difficult to elicit. The pupils were eccentric and contracted and reacted only slightly to light. The plantar reflexes were equivocal. His pulse was regular; respirations were gasping at a rate of 60 per minute. The patient's stomach was washed out, and an airway was inserted. Fifty milliliters of a 50% dextrose solution was given intravenously, and two further injections of 200 ml. of the solution were given 4 and 12 hours later. Oxygen was given by mask. A semicomatose condition persisted on the day following admission. On the fourth day, the patient was rational. The history of this patient revealed that in 1952 he had been admitted to another hospital after accidentally ingesting an unknown quantity of the same fluid.

The liver function tests showed no gross abnormality, and this is in agreement with observations by other workers, who have shown that trichloroethylene, unlike chloroform, carbon tetrachloride, and tetrachlorethane, to which it is chemically related, is not very toxic to the liver. Liver damage in industry has, however, been reported in poisoning by inhalation. Cardiac arrhythmia is sometimes observed when trichloroethylene is used as an anesthetic, and this patient showed definite but transient prolongation of the PR interval in the initial electrocardiogram and intermittent periods of rapid heart action. It is apparent that with adequate therapy complete recovery from trichloroethylene poisoning may take place despite long-continued coma.

THERAPEUTICS

Pancreatic Dornase Aerosol in Pulmonary, Endotracheal and Endobronchial Disease. E. E. Cliffton. Dis. Chest 30:373-384 (Oct.) 1956 [Chicago].

One hundred four patients were given inhalations of 100,000 units of pancreatic desoxyribose-nuclease (Dornase) dissolved in either 5 or 2 cc. of diluent; 2 or 3 cc. of the solution was administered with the aid of an aerosol inhaler using oxygen for nebulization. Sixty-five of the 104 patients were given pancreatic Dornase inhalations before local anesthetization in preparation for bronchoscopy, and the remaining 39 patients with uncontrolled pulmonary complications or disease were treated with pancreatic Dornase aerosol inhalations. Bronchoscopies were completed in 56 of the 65 patients, and 28 of these were ultimately proved to have carcinoma of the lung; 20 (71%) of the 28 had positive or suspicious results from cytological examination. None of the patients had false-positive results from the cytological examination. No untoward reactions to the pancreatic Dornase inhalations were observed in these patients. Of the 39 patients who were given pancreatic Dornase inhalations for treatment, 4 had lobar atelectasis, 4 had thick mucoid secretions and segmental atelectasis associated with serious chronic disease, 8 had thick tenacious sputum and/or segmental atelectasis or pneumonitis after thoracotomy with rib resection, 10 had advanced intrathoracic carcinoma, 3 were patients with tracheostomy, and 10 had miscellaneous conditions. Thirteen of the 39 patients were cured of the pulmonary complication or disease, 12 were permanently improved, 8 were improved temporarily, 3 were unchanged, and in 3 satisfactory evaluation of the results was not possible. Patients with acute pulmonary disease such as atelectasis secondary to mucus plugs or thick tenacious sputum responded most rapidly and satisfactorily to the pancreatic Dornase. Those with more chronic disease responded more slowly but remarkably well, while those with advanced malignant disease or chronic pulmonary disease with dry cough, such as postirradiation bronchitis, responded less satisfactorily or poorly to the drug. Even with repeated inhalations and repeated courses of inhalations, only a few patients had minor complications. Pancreatic Dornase would seem to be particularly useful in patients after thoracic surgery and in patients with post-traumatic thoracic injuries.

Sensitization and Subsequent Desensitization to Probenecid (Benemid). C. R. Austrian and W. P. Boger. A. M. A. Arch. Int. Med. 98:505-509 (Oct.) 1956 [Chicago].

A 65-year-old man with chronic tophaceous gout received 2 gm. of probenecid daily for 10 days and thereafter 1 gm. for an additional 20 days; a total dose of 40 gm. of the drug was given over a period of one month. No undesirable side-effects were observed. Ten months later, when treatment with the drug was reinstituted, marked itching of the feet, swelling of the face and scalp, and giant generalized urticaria developed within 30 minutes after the ingestion of a single dose of 0.5 gm. of the drug. Shortly thereafter there was profuse sweating, faintness, pallor, tachycardia, and a marked fall of blood pressure. These signs subsided gradually in the course of 12 hours after the administration of tripelennamine, but a moderate febrile reaction persisted for 24 hours.

In an attempt to desensitize the patient, whose sensitivity to probenecid was thoroughly established by the violent systemic response to the drug, an initial dose of 2 minims (0.12 cc.) of an aqueous solution of probenecid that contained 5 mcg. per cubic centimeter was given orally, and on each succeeding day thereafter the dose administered was increased in amounts of from 1 to 3 mcg. until 15 mcg. was given. Thereafter the increments were from 5 to 20 mcg. until the daily dose was 150 mcg.; this was increased daily by 250 mcg. until a dose of 2 mg. was reached on the 38th day. The patient then was given a daily dose of 15 mg. in capsules, and that amount was kept fixed for 10 days because of recurring mild urticaria, and for one day the amount administered was reduced to 7.5 mg. That the patient was sensitive to the chemical itself and not to some excipient in commercial tablets was thus confirmed. Thereafter the administration of the drug in encapsulated form was increased by 5 mg. daily until a dose of 75 mg. was reached, and then the rate of increase was about 10% daily, until, 99 days after the procedure was initiated, 2 gm. was given daily. After desensitization the patient was able to take the full probenecid dose with the expected benefits of such treatment, i. e., control of hyperuricemia, diminution and disappearance of established tophi, a decreased incidence of acute gouty attacks, and an increased sense of well-being.

QUERIES AND MINOR NOTES

HYPOMETABOLISM AND HYPOTHYROIDISM

To the Editor:—*A 27-year-old man 6 ft. 3 in. (190.5 cm.) tall, weighing 145 lb. (65.8 kg.), has been thin all his life, even though he eats well. He works long hours and has no specific symptoms, other than tiredness, which he attributes to the work and to lack of sleep. He has a basal metabolic rate of −29%. Would the administration of thyroid in small quantities be recommended?*

Manfred Thurmann, M.D., St. Louis.

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—It would seem that the administration of thyroid in this situation would be unjustifiable until further study of the patient was carried out and a true need demonstrated. Too frequently desiccated thyroid is given as a "therapeutic trial" and thus a sequence of injudicious management evolves without proved need. The taking of thyroid may "pep up" the individual, whether he is hypothyroid or euthyroid. He may thus be given a crutch he does not need. Suppression of the normal thyroid function will occur, and a true physiological, but temporary, hypothyroid state will occur when an attempt is made to withdraw the thyroid medication. Such therapy once started makes the original uncertainty more difficult to clarify.

Certain matters in this case need clarification. If there are no other symptoms or physical findings suggesting thyroid insufficiency, one might be skeptical of the need for thyroid medication. There is a difference between secondary fatigue resulting from excessive work and insufficient rest and primary fatigue that hampers the individual's ability to work. Does rest have any effect on this man's fatigue? A short therapeutic trial might be useful.

The determination of basal metabolic rate, the only test used here thus far, may be decidedly misleading. Although false-high results are more common than false-low results, it would be wise to repeat the test. The first determination is often particularly misleading. Since the basal metabolic rate at hand is not supported by the clinical impression, a second laboratory (where many tests are run) should be selected. One reason for a low basal metabolic rate is constitutional thinness, which might be the explanation for the reported result in this patient. If the low basal metabolic rate is confirmed, further tests are indicated. Tests for either radioactive iodine (I^{131}) uptake or protein-bound iodine level, or both, should be performed. These tests are also subject to error, but the three should certainly clarify the issue with considerable finality. The cost in time and money to the patient will be far less than that resulting from prolonged medical attention, which will evolve if the patient is unjustifiably tagged with a diagnosis of thyroid insufficiency.

Answer.—In a patient with a basal metabolic rate of −29% the test should be repeated several times, to be sure of accuracy. If the metabolism continues in this low range in an otherwise apparently normal 27-year-old man, it may suggest hypometabolism, in which case, a trial of therapy with triiodothyronine, 25 mcg. two times daily for two to three weeks, should be given, after which the metabolic rate should be rechecked. Determination of serum protein-bound iodine level as well as cholesterol level would help ascertain whether the patient is hypothyroid or has hypometabolism. Desiccated thyroid would be of benefit if the patient has hypothyroidism but would be of little, if any, benefit if the patient has hypometabolism. In hypometabolism, the serum protein-bound iodine level and the serum cholesterol level are normal and the metabolic rate continues to be low. In hypothyroidism, either primary or secondary, there is a decrease in the serum protein-bound iodine level as well as a low basal metabolic rate and the serum cholesterol level is usually elevated.

APPEARANCE OF A SIGNIFICANT Q WAVE

To the Editor:—*When a Q wave develops as a result of myocardial infarction, is it permanent? What conditions can bring about a change in a Q wave? The patient whose case prompted this question is 60 years old and had the clinical appearance of a mild myocardial infarction with precordial pain radiating to the left arm. The electrocardiogram showed Q waves in leads 3 and AVF as the only change from a previous record taken eight months before, and a posterior wall infarction was diagnosed. However, a few days later these Q waves had disappeared and acute cor pulmonale was then diagnosed, supported by such clinical signs as rales in the left lung and a small pleural effusion on x-ray. However, two weeks later, the Q wave reappeared in leads 3 and AVF and deeply inverted T waves in V5 and V6; the T waves seemed typical of the evolution of an infarct. The stumbling block in the diagnosis of an infarct, in my opinion, is the period when Q waves were absent.*

M.D., Connecticut.

Answer.—The appearance of a significant Q wave in the electrocardiogram in a lead in which it did not previously exist brings to bear strong evidence to support the diagnosis of myocardial infarction. The Q wave occurs because of the presence of electrically inactive tissue beneath the electrode in the case of a so-called unipolar lead or in the plane of electrical activity in a bipolar lead. The appearance or disappearance of a Q wave in lead 3 alone is of minor significance. However, when such a change is associated with the appearance of a Q wave in AVF, there exists strong evidence of the presence of a posterior myocardial infarct. Lead AVF is inscribed from an electrode that faces the posterior-inferior (diaphragmatic) surface of the heart. If the position of the heart be altered, with respect to the electrode, the portion of the heart that faces the electrode will be a different one. The position of the heart may be altered by a difference in the position of the patient at the time of different electrocardiograms, by the presence of pressure from below the diaphragm (ascites, distention of the intestine), by an altered pressure in the mediastinum (pneumothorax, atelectasis), or by an infarct of the myocardium that causes the altered muscular contraction to produce cardiac rotation. If any of these phenomena produced a change in the relationship between the surface of the heart and lead AVF, the pattern of AVF might well be altered. When any of these causes becomes adjusted, the original pattern of the electrocardiogram is likely to be restored. In the present case, the later development of T wave changes in V5 and V6 strongly suggests the presence of a posterolateral infarct.

FEEDING GARBAGE TO PIGS

To the Editor:—*In some states garbage has to be cooked before it is given to pigs. Do pigs get food poisoning when they eat spoiled meats and vegetables and rancid fats? What about broken glass and bottles? Frequently when we have a run of ants in garbage, chlordane ant powder is put in and around the garbage can. What happens when pigs eat this and other poisons in garbage?*

M.D., California.

Answer.—The problem of feeding raw garbage to swine has, in the past, presented economic and public health problems. Studies have indicated that swine have become infested with Trichinella and infected with virus causing vesicular exanthema due to the consumption of raw garbage. Studies made by the United States Department of Agriculture indicate that the eradication of vesicular exanthema would be impossible as long as the practice of feeding raw garbage to swine is con-

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

tinued. At present 46 states require that all garbage be cooked at a temperature of 212 F for 30 minutes. The effective cooking of garbage destroys all viruses and pathogenic organisms and prevents illness of swine and the subsequent economic loss due to death of animals.

A search of the literature failed to indicate data as to the effect of the use of poisonous insecticides on garbage that is subsequently used for hog feeding. However, where garbage from many sources is combined and cooked prior to feeding, the problem would be minimal, due to the reduction in the concentration of the economic poison to a point far below toxic limits. All users of garbage destined for swine feeding require separation of glass and metal from the garbage prior to collection. Glass and metallic particles are heavier than the organic wastes comprising garbage and therefore lend themselves to easy separation during the garbage cooking operation. Removal is effected either through apertures in the base of the cooking vat or by utilizing a simple trap in the vat.

METASTASIS OF BREAST CARCINOMA

To the Editor:—*A radical mastectomy was performed for carcinoma of the left breast in a woman 35 years of age who had delivered her first child one week before the operation. She noted the lump on the medial aspect of the breast about two weeks before delivery but did not tell her physician about it until just after delivery. There were no positive nodes in the left axilla. The case was discussed with a radiologist, and it was decided that x-ray therapy would probably be of no avail. Eight months later a nodule was palpated in the right axilla. Frozen section showed this to be a metastatic lesion, and a radical right mastectomy was performed. There was no evidence of carcinoma in the right breast clinically or by microscopy, but positive nodes were found in the right axilla. A preoperative x-ray of the chest showed a small suspicious but not definite area in the mediastinum. The lung fields were clear. A bilateral oophorectomy was performed one week after the second mastectomy. Should she have x-ray therapy now, or should she wait for definite evidence of metastasis? If it is advisable to use x-ray therapy now, where should it be given and what dosage would be prescribed?*

M.D., Pennsylvania.

Answer.—Nothing should be done for the present, until the effects of the oophorectomy can be appraised. If localized metastasis appears, x-ray therapy may be tried to the area. If widespread metastasis occurs, a trial of therapy with cortisone, 100 mg. daily, should be given and continued as long as there is benefit. When any beneficial effects of the above treatments are gone and the patient is in relapse again, a hypophysectomy should be done.

NEURALGIA AFTER LAMINECTOMY

To the Editor:—*A patient had a laminectomy 10 months ago for intractable pain. A degenerated disk was found at the fifth lumbar vertebra and removed. She has since been relieved of sciatica but has developed a burning and neuralgic type of pain along the femoral and sciatic nerves of the right leg. A neurosurgeon felt that this was due to inflammation of nerve roots and associated spasms and would be many months in resolving. The reflexes returned to the affected leg and skin sensation is normal. He did not feel that there was any nerve root compression. He gave her Arlidin, which would help to relieve the spasms. She requires ¼ grain (15 mg.) of morphine every day or so to remain free of pain. If this is withdrawn, she exhibits no withdrawal symptoms and the pain will diminish after a few days of absolute bed rest. Please give suggestions as to the treatment and prognosis of this neuralgia.*

James D. Wilson, M.D., Greenville, Miss.

Answer.—The return of reflexes and sensation would indicate that there is very little if any nerve root compression, and one would then project a good eventual prognosis. If the pain disappears on bed rest, a factor in its etiology is probably a weak musculature. This could be overcome by postural exercises. The most important would be straight leg raising while lying on one's back, with the hope of strengthening the abdominal muscles. Assuming a posture that removes the lumbar lordosis is a goal toward which to strive. The exercises and posture should become a part of the morning ritual. Analgesics such as aspirin should be substituted for narcotics, and a brief trial of therapy with a tranquilizing drug could be considered.

SUDDEN LOSS OF VISION

To the Editor:—*A 39-year-old woman, mildly hypothyroid, taking 2 grains (0.12 gm.) of thyroid daily, had sudden partial loss of vision in the left eye. Examination showed that, where there was previous 20/20 vision, there is now 20/30 in that eye. There was occlusion of the inferior temporal retinal artery just below the area of the macula. The suggestion of a vasospasm, or thrombus, was considered. The patient showed edema typical of an infarct, extending almost to the macular area. Five days prior, she had had dental work done on the same side of her face, with various deep injections of Novocain in the area behind the left tonsil and at the inside junction of the mandible. There is tenderness of the left side of the neck directly below the angle of the jaw on the same side. The patient was given an injection of Depo-Heparin and vasodilators four times a day, and there has been no change of her condition. The questions are as follows: 1. What is the acceptable treatment in this type of case, other than that already given? 2. What is the prognosis?*

Albert C. Esposito, M.D., Huntington, W. Va.

Answer.—Usually, when a vasospasm or arterial closure has existed for a few days, there is no treatment of value. If the patient were seen extremely early, perhaps the retrobulbar injection of Priscoline or acetylcholine would be of value. Amyl nitrite inhalations have been recommended, as have ocular massage, paracentesis of the anterior chamber, and other measures designed to lower the intraocular pressure.

MILD HYPERTHYROIDISM

To the Editor:—*Is it advisable for a 22-year-old boy to study a profession, such as engineering or optometry, if he has mild hyperthyroidism? His symptoms are exophthalmos and nervousness. There is no relief from iodine therapy. The diagnosis of hyperthyroidism was made after a complete physical examination.*

M. D., Florida.

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—In view of the persistent symptoms presented by this young man, it is suggested that further study be made to rule out the potentiality of some conditions other than simple mild hyperthyroidism. A consultation at this time might indicate another diagnostic possibility or the desirability of some other form of therapeutic approach than the utilization of iodine. Mild hyperthyroidism under adequate therapeutic control should not contraindicate study for a professional career.

Answer.—Hyperthyroidism is a correctable disease. There is no reason why it should not be controlled within a period of three or four months at the most, and there is no reason why recovery should not be complete. Alternative methods of treatment are the use of the antithyroid drugs, radioactive iodine, or thyroidectomy. One would not expect complete and sustained relief from iodine therapy alone in the majority of cases. There is no reason why the presence of hyperthyroidism should in any way interfere with a boy's career.

CHOKING ON FOOD

To the Editor:—*What is the treatment for choking on food while eating, when food has entered the trachea and the patient is in acute distress with cyanosis and dyspnea?*

Rowland P. Stanley, M.D., Garden Grove, Calif.

Answer.—Aspiration of a foreign body into the trachea, occurring most frequently during infancy and early childhood, commonly produces only partial obstruction of the respiratory tract. These objects are managed best by bronchoscopy and removal. Conservative treatment of foreign bodies within the trachea is not warranted, since only rarely (less than 5% of cases) will a foreign body be evacuated spontaneously. Actually, a progressive inflammatory reaction within the tracheobroncheal wall usually fixes the food particle in its aberrant position. The uncommon occurrence of cyanosis and dyspnea due to complete obstruction of the airway immediately after aspiration requires emergency tracheostomy to avert the patient's death. Here any firm tubing, such as a fountain pen top, may be passed into the trachea by way of a vertical incision through the skin and the second or third tracheal cartilage for an airway. With restoration of respiration, the foreign material can be removed shortly at endoscopy. Thoracotomy and bronchoscopy should be reserved only for the rare cases where all attempts at bronchoscopy have failed to remove the object.

EFFECT OF ILEOSTOMY ON PREGNANCY

To the Editor:—*What are the chances of pregnancy for a 29-year-old woman who has an ileostomy following abdominal perineal resection due to ulcerative colitis at the age of 24? The ileostomy was revised in 1954. The patient now is apparently healthy and plays golf and tennis and swims. She works normally and has been happily married for two and one-half years. Will pregnancy influence her ileostomy? This patient, with type B, Rh-negative blood, was given Rh-positive blood by mistake.* T. T. Tchen, M.D., Baltimore.

Answer.—The term "chances of pregnancy" might be taken to mean either the patient's ability to conceive, or the likelihood that a gestation will progress without special complications. As to the first question, there is the possibility that peritoneal adhesions, resulting from the colitis or from the extensive surgery performed, may have sealed the tubes or interposed adhesions between them and the ovaries. As to the second, this consultant thinks that serious difficulties would not be encountered. Both the abdominal wall and the viscera adapt themselves remarkably well to the altered mechanical conditions created by the growing uterus. If the patient's husband is Rh negative, no harm can come to her baby, and trouble is not inevitable if he is Rh positive and heterozygous. But if he is Rh positive and homozygous (the chances of this are about 50%), then the titer of Rh antibodies in her blood, probably low at present, is almost certain to rise during pregnancy and may well reach a level at which the baby will be gravely endangered.

PROSTATIC HYPERTROPHY NOT RELATED TO SEX HABITS

To the Editor:—*Are there any extensive studies of the sex habits of men who have prostatic hypertrophy? Is there any correlation between the number of emissions during the 10-to-30-year period prior to the time the prostatic hypertrophy becomes clinically evident?* R. R. Grayson, M.D., Perryville, Mo.

Answer.—Extensive studies of the sex habits of men in regard to hyperplasia of the prostate have been made and recorded. There is no evidence that sexual activity per se and the activity of sex as such has any influence on the development of prostatic hyperplasia. There is a marked racial difference in the development of prostatic hyperplasia, as evidenced by its low incidence in the Oriental and by its almost nonexistence in certain parts of Africa among the Negro race. Whether this is due to an endocrine influence is not known, but it is more probably due to that than to any activity of the glands themselves. The incidence of prostatic hyperplasia in so-called celibates is practically the same as it is in married men, who have supposedly enjoyed a normal sex life.

BLOOD CHOLESTEROL

To the Editor:—*Please tell me what influence tumors of the kidney or adrenals might have on persistent hypercholesteremia. What do you consider the normal range of cholesterol in the blood?* M.D., New Jersey.

Answer.—Tumors of the kidney are not known to produce any effect on serum cholesterol levels. Tumors of the adrenals, or hyperadrenalcorticalism, i.e., in Cushing's disease, are associated with hypercholesteremia. Treatment with hormones of the adrenal cortex, or corticotropin, according to some authors is accompanied by hypercholesteremia. However, others report no significant changes even after the prolonged administration of these hormones. The normal value for blood cholesterol in the United States according to Peters and Van Slyke is from 180 to 310 mg. per 100 cc. However, most workers in this field in recent years consider 260 mg. per 100 cc. as the upper limit of normal.

EPINEPHRINE AND REPOSITORY CORTICOTROPIN INJECTION CONTRAINDICATED IN SAME SYRINGE

To the Editor:—*Is there any incompatibility between epinephrine, 1:1,000 (0.3 cc.), and repository corticotropin injection (corticotropin gel), 40 U. S. P. units per cubic centimeter, mixed in the same syringe to be given intramuscularly for asthma?* Jacob Greenblatt, M.D., Stamford, Conn.

Answer.—There is no chemical incompatibility between epinephrine solution and repository corticotropin injection. However, there are at least two objections for this combined form of therapy. The added solution of epinephrine dilutes the repository corticotropin injection so that the effect of prolonged absorption from the latter may be disturbed. Epinephrine is designed for the immediate relief of the asthma, corticotropin for the more remote effect. Both drugs could be given at the same time (but not in the same syringe) only if the effect of each is required.

SWALLOWING AND ASPIRATION OF CHEWING GUM

To the Editor:—*What are the consequences if someone accidentally swallows chewing gum? Have cases been reported where chewing gum was accidentally aspirated?* Ernest Spitzer, M.D., St. Louis.

Answer.—Records have not been found of any unpleasant happenings after the accidental swallowing of chewing gum. This undoubtedly happens frequently in our gum-chewing population, particularly among children. Accidental aspiration is, of course, possible, and the consequences are the same as those occurring in the aspiration of any foreign body. Frequent and deliberate swallowing of chewing gum could conceivably cause a phytobezoar in the stomach. However, it is difficult to conceive of any unpleasant effects from the occasional, accidental swallowing of chewing gum.

TOMATOES AND STRAWBERRIES

To the Editor:—*What is the consensus concerning the ingestion of tomatoes and strawberries by healthy individuals? Is there any truth in the widespread belief that the former are cystotoxic and the latter nephrotoxic?* M.D., New York.

Answer.—The tomato, like the potato, is a member of the nightshade family, and, perhaps because this family is known to include several poisonous plants, the tomato was held in suspicion until the middle of the 19th century. Because the strawberry has produced hives in some persons, it, too, has been regarded with suspicion. Physicians today agree that the ingestion of tomatoes and strawberries by healthy persons is not harmful.

METALLIC TASTE IN THE MOUTH

To the Editor:—*Please discuss the cause and treatment of a metallic taste in the mouth. I have had several patients with this complaint whose teeth and mouth are normal.* R. W. Lieber, M.D., Durand, Mich.

Answer.—The cause of metallic taste in the mouth is frequently due to infection in either the nasopharynx or decayed teeth. In rare instances an allergy to food or tobacco has been described. Also, in rare instances the presence of adjacent silver and gold fillings has caused a metallic taste. However, an emotional basis is the usual cause. Investigation of emotional problems is indicated. Sedatives such as phenobarbital or the newer tranquilizers have proved successful in many cases.

« Washington News »

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SECRETARY FOLSOM OUTLINES HEALTH GOALS

In several public addresses prior to the opening of Congress, Secretary Folsom gave indication of what the administration will ask of the 85th Congress in the health field. The administration's 1957 legislative goals will be outlined by the President in his State of the Union message scheduled for delivery in January. The Secretary of Health, Education, and Welfare says the administration will ask for funds to help medical schools build classrooms. During the last session the administration requested 250 million dollars for a five-year program of grants for laboratory facilities and classrooms. Congress appropriated instead 90 million dollars for three years, limited to research facilities. "We are going to recommend again that they expand that to bring it up to the full $250 million to include both teaching and research facilities because the medical schools not only do much with medical research but they train the scientists and the doctors," he declared.

As another means of encouraging expansion of voluntary health insurance, the administration will again ask Congress to authorize pooling arrangements between smaller insurance companies so that they might expand coverage. Late in the last session, Mr. Folsom's department sponsored a bill to waive antitrust laws for these companies, but it was introduced too late for action. In recent weeks Mr. Folsom has cited rapid gains being made in voluntary insurance covering major medical expenses, generally after the first $100 has been paid by the insured. When coupled with basic coverage, catastrophic insurance affords a family adequate protection, he has poined out.

Mr. Folsom also has indicated the department will ask for more funds for the next fiscal year than the 2.2 billion dollars voted by the last Congress. That figure included 1.3 billion dollars to the states for public assistance. Taking cognizance of the possibility of new demands on the budget for defense purposes, Mr. Folsom declared: "While we must maintain this defense posture . . . we want to be very careful that we don't let down on expenditures in the field of health, education, and welfare. . . . We have got to look out for our human resources." On social security changes, Mr. Folsom said the administration felt there was no need for any action, at least on old-age benefits.

PILOT PROJECTS FOR STUDY OF FACILITIES

A government advisory committee has requested that hospitals set up a number of pilot projects through which a study could be made of facilities and services for patients who need only limited care. The committee, appointed in September by Secretary Folsom and headed by Dr. Russell Nelson of Johns Hopkins Hospital, made its recommendations after reviewing preliminary facts assembled by the Department of Health, Education, and Welfare. Of the proposed hospital projects, the committee says: "These new types of units would be designed to provide a basis for further study of ways to improve care for these patients, perhaps at lower costs than would otherwise be possible."

Dr. Nelson says the committee at present is confining its consideration to the needs of three specific groups of patients: (*a*) those convalescing from acute illness, (*b*) those convalescing from chronic illness, and (*c*) those requiring only diagnostic services and facilities.

On long-range objectives, Dr. Nelson declares: "The aim of the committee is to obtain from the pilot studies practical recommendations which can be adapted with minimum cost by virtually any hospital or community to establish facilities for patients needing only limited care. On the basis of these findings, we hope agencies concerned with hospital and medical care—especially voluntary agencies—will be better able to develop similar facilities and services to meet their own needs."

NEW SOURCE FOR CORTISONE

A plant that grows in profusion in parts of Texas and is often fatal to sheep and goats promises a new, cheap, and entirely domestic source for cortisone. The Department of Agriculture, identifying the plant as Agave lecheguilla, gives this explanation: "This unwanted weed is the most promising native plant yet found to yield substances that can be converted to cortisone. . . . Chemists of USDA's Agricultural Research Service have discovered in the plant a substance known as smilagenin, from which cortisone can be made by chemical means. Although higher yielding plant-sources of cortisone-like drugs have been found, this one is potentially important because it grows in such profusion within the nation's borders. It covers thousands of square miles in the Big Bend region of Texas."

PRESENT PLENTIFUL SUPPLY OF SALK VACCINE

President Eisenhower has joined Secretary Folsom in urging young adults to have Salk vaccine injections immediately in an effort to reduce the incidence of poliomyelitis next season. Secretary Folsom reported to the President that at present 17,000,000 doses of the vaccine are lying unused in drug manufacturers' ware-

(*Continued on page 23*)

From the Washington Office of the American Medical Association.

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DIGOXIN
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A pure, stable, crystalline glycoside isolated from Digitalis lanata...

(cont'd) ↗

BURROUGHS WELLCOME & CO. (U.S.A.) INC., Tuckahoe, New York

Washington News—Continued

houses. In addition the vaccine is stockpiling in drugstores and doctors' offices. Besides urging the inoculation of young adults, the Secretary recommended that "millions of children who have so far received only one or two injections should be given the additional protection provided by the recommended three doses."

Today, Mr. Folsom pointed out, the large supply of Salk vaccine provides the way to prevent paralysis or even death. The present danger is public apathy, which can be overcome by "earnest and vigorous cooperation of parents, physicians, schools, officials at all levels of government and public and private health agencies."

Recently the Commerce Department approved the export of 29,300 doses of Salk vaccine for Hungarian refugees. The shipment, enough to inoculate about 15,000 children and young persons, is being rushed to Vienna for distribution by the International Rescue Committee. The Pitman-Moore Company of Indianapolis donated the vaccine.

MEDICAL CARE COSTS

Medical care costs, which are computed in the nation's cost of living figures, rose 1.5% during the third quarter of this year, according to the Bureau of Labor Statistics. Fees charged by physicians, however, rose only 0.8% during the three-month period ending in September, the government agency reported. The over-all increase in the cost of living was 0.7% for the period.

The Bureau of Labor Statistics said medical care costs when drugs were excluded increased 0.9% in the third quarter. Fees charged by surgeons showed one of the smallest increments: 0.5%. General practitioners' fees rose 0.8% while obstetric care was up 1.7%. Major factors in bringing the over-all medical care index higher during that period were a 3.2% rise in hospital rates and a 3.9% increase in group hospitalization fees. Prescriptions and drugs rose 0.7% and dentists fees, 0.16%.

BUSINESS AND A REHABILITATION PROGRAM

Private business cannot "sit smugly back and assume that some governmental agency or institution will find the way" to rehabilitate the rapidly increasing number of disabled persons, according to an article in the U. S. Chamber of Commerce publication, American Economic Security.

The author, W. Scott Allan, points out that the present statistics of the National Safety Council list 1,900,000 work accidents in 1955 with a cost in labor hours and medical expenses of 3.5 billion dollars. The Bureau of Labor Statistics estimates that between 5 and 6 million persons of working age in the United States have disabilities that hinder their finding jobs.

The future trend "toward including the degenerative conditions, such as heart disease, arthritis and the like, under workmen's compensation, together with the recognized aging of our general as well as our working populations, means greater burdens for industry and insurance in the future," the author writes.

Mr. Allan finds that the solution to the problem is a sound rehabilitation program with business interests the focal point of community planning. Industry must train personnel officers to understand the injured worker's needs and capabilities. Community planning, plant programs, and educational campaigns can help achieve "restoration of a disabled individual to a useful and productive life . . . a goal which is economically and socially sound."

INTERNATIONAL SCIENTIFIC CONFERENCE

An international conference on scientific information is scheduled for November, 1958, in Washington, D. C., under sponsorship of the National Science Foundation, the National Academy of Sciences–National Research Council, and the American Documentation Institute. Preliminary plans for the session were made at a meeting of 50 scientists and experts in documentation, meeting at the National Academy of Sciences in Washington. Participation will be restricted to specialists in the fields to be covered by the agenda, but observers will be welcomed if they register in advance. The plan is to limit the delegate list to 150, including authors of papers and members of review panels. Copies of all papers will be mailed to delegates at least two months in advance of the conference.

PENSONNEL

Paul B. Murphy, food specialist with the Bureau of Indian Affairs, will direct an American Red Cross program for feeding Hungarian refugees. He already is on duty in Salzburg, Austria. . . . Senator Bricker is preparing a new version of his amendment, for which he will ask White House support. The objective is to forbid the signing of treaties that interfere with state or local rights. An earlier version, opposed by the Eisenhower administration. lost out in the Senate in 1954. . . . Major Gerald Champlin is the first Army doctor to complete a course at the Navy Deep Diving School. The ultimate objective is to provide Army divers with doctors who understand the special medical problems of deep-sea diving.

MISCELLANY

The first federal old-age and survivors insurance checks have already reached 300,000 women in the 62 to 64 age group. They became eligible for payments under the recent amendment to the social security law lowering the age from 65. . . . The VA advises that the best Christmas gifts for veterans who will spend the holiday season as patients in Veterans Administration hospitals are visits from friends and relatives or a long letter from home. . . . The Navy Bureau of Medicine and Surgery is planning a symposium late in January to acquaint field representatives with Bureau policy and the Bureau with field problems. . . . Two Public Health Service scientists, Drs. Daniel Steinberg and Donald S. Frederickson, report they have found a way to control in laboratory animals the natural production of cholesterol.

(cont'd)

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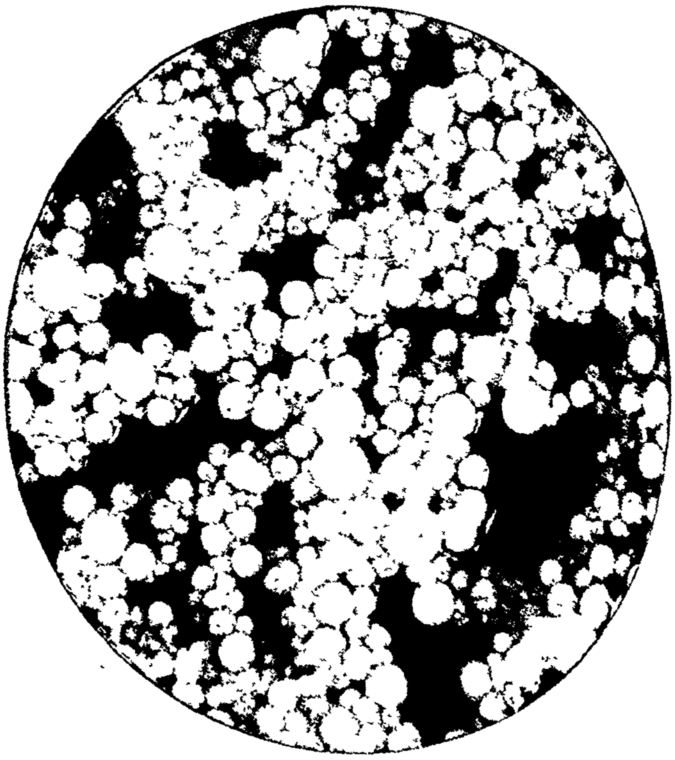

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THE JOURNAL

of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 162, NO. 16

CHICAGO, ILLINOIS

DECEMBER 15, 1956

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ADVANCED MAMMARY CANCER TREATED WITH SEX HORMONES

Edward F. Lewison, M.D., Frances H. Trimble, M.D.
and
Robert S. Ganelin, M.D., Baltimore

• *Estrogens were compared with androgens as to their effects on 133 patients with advanced mammary cancer. Estrogens should not be used for this purpose in women less than five years past the menopause; when properly used they were found to be somewhat superior to the androgens in their objective effects on lesions in soft tissues and viscera. The androgens were somewhat more potent by subjective critera. Both androgens and estrogens gave a sense of well-being and partial or complete relief of pain in about half of the patients. Regression of the tumor sometimes occurs also upon discontinuation of hormone therapy that has been ineffective or has ceased to maintain an initial improvement. Full use should be made of these profound and gratifying palliative effects of hormone therapy.*

Mammary cancer is an all-too-common universal tragedy—malign and monstrously destructive of human life. Morbidity studies for each sex in the United States[1] indicate that the age-adjusted incidence rate for cancer of the breast is considerably higher than for any other specific primary site. The breast is by far the most frequent single female organ attacked by cancer. The incidence of mammary cancer represents 21.7% of all cancers in females, and it is the leading cause of death among women in the midperiod of life, from 40 to 60 years of age.[2] It is readily apparent that in the total care of mammary cancer the palliative treatment of advanced, recurrent, and metastatic disease by means of hormone therapy has become a problem of major magnitude in clinical management. The purpose of this presentation is to describe the results of sex steroid therapy in a series of patients with this disease.

Historical Review

The intimate relationship between the breasts and ovaries was recognized without being understood for many years before the isolation of the sex hormones and the elucidation of the complex pattern of endocrine interrelationships. The earliest reported attempts to influence mammary carcinoma by physiological means were described by Beatson[3] in 1896. He had become interested in lactation in 1876 and, having observed that the cellular proliferation and desquamation of lactation were associated with a temporary cessation of ovarian activity, he hoped that a similar degeneration of epithelial cells would follow removal of the ovaries. To reinforce this effect, he administered thyroid extract to his patients postoperatively. This method of treating recurrent carcinoma of the breast was followed in Britain for many years, but, as it was never endorsed with any enthusiasm by the influential German school, its popularity waned. At a later date, castration by the simpler method of irradiation was reintroduced and in some clinics is employed as a routine in premenopausal patients with axillary metastases at the time of operation.

Meanwhile, experimental work on ovarian function was proceeding, due to the impetus given by Lathrop and Loeb,[4] who demonstrated first in 1916 the decrease in incidence of spontaneous mammary carcinoma in mice after oophorectomy. During the next decade, progress was made in the isolation of the ovarian hormones as well as in the recognition of the various components of the pituitary complex. Administration of these hormones to experimental animals suggested a cause-and-effect relationship between estrogens and mammary carcinoma, a relationship that could sometimes be altered by the use of androgens. Loeser was the first to use this observation clinically and administered androgens postoperatively to patients with mammary cancer and a strong family history of carcinoma. The dramatic results obtained in the treatment of prostatic carcinoma by castration and estrogen therapy, as outlined by Huggins and Hodges,[5] stimulated interest in this new form of chemotherapy.

The employment of estrogens in the treatment of carcinoma of the breast appears paradoxical and stems from the observations of Haddow[6] in 1935 that certain benzanthracene derivatives, already shown to have carcinogenic properties, dramatically inhibited a cer-

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From the Breast Clinic, Division of the Tumor Clinic, Department of Surgery, Johns Hopkins Hospital and Johns Hopkins University.

tain type of rat tumor. Zondek, a pioneer in the field of endocrine physiology, in 1936 suggested the use of estrogens in breast carcinoma in an effort to suppress the secretion of gonadotropins and the growth hormone (somatotropin) from the anterior pituitary. Scattered reports of experience with estrogen therapy appeared from various centers in Britain and the United States over the years, with results that were sufficiently encouraging for experimentation with the newer compounds to continue.

The more recent approach to the problem of altering the hormone pattern really begins where Beatson left off. It has been demonstrated both in experimental animals and in human subjects that in time adrenal hyperplasia follows oophorectomy. Estrogens are produced by the adrenals, and frequently progression of the disease follows. Huggins and Bergenstal[7] suggested bilateral adrenalectomy to eliminate this secondary source of estrogen production, and about 40% of patients undergoing that procedure, mainly those who have responded favorably to oophorectomy originally, show a good but temporary response. A less formidable method of achieving a similar result is by giving cortisone, a method that is receiving careful investigation at the present time. The most recent approach, and one that appears more logical, is the operation of hypophysectomy, whereby the source of both gonadotropins and somatotropin is eliminated. The present status of this operation, with a review of about 50 patients, has recently been presented by Kennedy, Peyton, and French.[8]

Mode of Action of Sex Hormones

As is well known, the hypophysis, or pituitary gland, regulates the endocrine system of the body and is itself controlled by the hypothalamus. Throughout the reproductive years there is a delicate balance between the production of gonadotropins from the hypophysis and the sex steroids from the gonads. The reproductive system, which includes the breasts, is normally controlled by the follicle-stimulating hormone (FSH), luteinizing hormone (LH), and prolactin produced by the pituitary and the gonadal hormones estrogen, androgen, and progesterone.

In general, any increase in the amount of a particular pituitary hormone (or tropin) will lead to hyperplasia of the target gland and an increase in production of its hormones. Conversely, a deficiency in the amount of a given tropin will result in atrophy of the target organ. The administration of a target gland hormone inhibits the production of the corresponding tropin and usually alters the production of other pituitary hormones. For example, the administration of thyroid extract inhibits the secretion of thyrotropin and the follicle-stimulating hormone and stimulates the production of the other tropic hormones. The administration of testosterone inhibits the production of gonadotropic and adrenotropic hormones; an excess of estrogens inhibits the production of follicle-stimulating hormone but stimulates that of luteinizing hormone and prolactin. All cells in the body are affected by the thyroid and growth hormones, whereas the gonadal hormones influence specific metabolic processes and tissues, chiefly the reproductive system.

When castration is performed in the premenopausal subject, there is a sudden withdrawal of estrogenic compounds. Frequently this leads to a dramatic improvement in the clinical course of mammary cancer, an improvement that may persist for several months or more. However, the operation is followed by hypertrophy of the adrenals and enlargement of the pituitary gland. The adrenals are stimulated to produce estrogens by an increase in gonadotropins, and a direct stimulation of the tumor is probably produced by the increased amounts of growth hormone.

The initial effect of the absence of estrogens is to ensure a preponderance of androgens, which favors protein synthesis and osteogenesis. There is also stimulation of hematopoiesis. These same effects are obtained when androgens are administered therapeutically, as in the premenopausal patient. With the androgens acting through the pituitary, a chemical castration occurs and amenorrhea soon develops. Estrogens, however, do not completely disappear from the urine during this therapy and may be a product of androgen metabolism. The precise mode of action of the estrogen therapy used in postmenopausal patients is still not clear, but Nathanson has stated that estrogens act directly on the disease, whether in bone or in soft tissues, and that calcification and osteogenesis are secondary metabolic effects. In patients with advanced cancer of the breast tracer studies using sodium estrone sulfate labeled with radioactive sulfur (S^{35}) indicated a concentration of radioactivity in the tumor tissue.

The effect of castration, androgen, or estrogen therapy may be, as Nathanson suggested, to effect a "chemical hypophysectomy." Undoubtedly, a profound change is induced in the physiological status of the patient whereby for a time the host becomes less vulnerable to the spread of her disease and the tissues "less fit food for the cancer protozoan," as Hermann[9] postulated in 1898 in discussing oophorectomy. According to our present knowledge, this stage is time-limited and extremely variable.

Clinical Material

This study is part of a program of collaborative clinical research coordinated and sponsored by the Committee on Research of the Council on Pharmacy and Chemistry of the American Medical Association. The clinical material comprising this investigation consists of 133 women with inoperable, recurrent, or metastatic mammary cancer who received a total of 223 complete courses of hormone therapy at the breast clinic of the Johns Hopkins Hospital between June, 1947, and August, 1955.

The requisites for inclusion in this clinical investigation were formulated by the Subcommittee on Steroids and Cancer of the Committee on Research and were strictly adhered to in reporting these results. Only patients conforming to the following criteria were considered eligible for this study: First, the diagnosis of cancer of the breast must have been established by microscopic examination in all patients. Second, all patients must have had inoperable, recurrent, or metastatic disease that was no longer amenable to accepted surgical and radiotherapeutic measures. Radical mastectomy and radiotherapy are generally regarded as the treatment of choice in cancer of the breast. Patients considered "curable" by these conventional methods of therapy were not denied such measures in favor of chemotherapeutic palliation. Third, patients must not have received surgical or radiotherapeutic castration within six months prior to the onset of hormone therapy, as castration itself has long been known to be of benefit in the palliative treatment of mammary cancer. Fourth, patients must not have received radiotherapy to any lesion under observation within six months prior to the onset of hormone therapy. However, a few patients with generalized metastatic disease who received limited irradiation to local lesions were retained in the study. In these patients, only the nonirradiated lesions were observed and evaluated for their response to hormone therapy. Thus, the results of this study are believed to be independent of the effects of either castration or radiotherapy. Fifth, the minimum period of uninterrupted hormone therapy required for evaluation of results of an individual course was eight weeks. This period has been regarded as an adequate minimum time to estimate by therapeutic trial the initial effectiveness of a particular sex steroid. While some patients had only the minimum 2 months of therapy, others had continuous treatment lasting as long as 44 months. No effort was made to evaluate the results of therapy in relation to the length of time of treatment, although it is known that total dose and duration of treatment are both important. Patients who were recorded as having received more than one course of estrogens might have received the same hormone at two different periods separated by an interval of time.

Table 1.—*Treatment Schedule of 133 Patients Receiving 223 Complete Courses of Hormone Therapy*

Drug and Route	Dose	Complete Courses of Treatment, No.	
Oral			
Ethinyl estradiol	3 mg. daily	50	110 courses of androgen therapy
Chlorotrianisene (TACE)	24 mg. daily	41	
Diethylstilbestrol	15 mg. daily	9	
Parenteral			110 courses of estrogen therapy
Testosterone propionate in oil	25 mg. 3 times weekly	14	
	50 mg. 3 times weekly	3	
	100 mg. 3 times weekly	36	
	200 mg. 3 times weekly	9	
Stanolone	100 mg. 3 times weekly	17	
Testosterone cyclopentylpropionate	100 mg. once weekly	12	
Dihydrotestosterone cyclopentylpropionate	100 mg. once weekly	3	
Methylandrostenediol	100 mg. 3 times weekly	2	
Oral			
Methyltestosterone	50 mg. daily	3	
	100 mg. daily	5	
	200 mg. daily	6	
Combined therapy			
Ethinyl estradiol plus progesterone		4	13 courses of combined therapy
Ethinyl estradiol plus chlorotrianisene		1	
Ethinyl estradiol plus testosterone propionate		8	
Total		223	

Two months was carefully selected as a sufficient trial period because patients who show an objective response to therapy will do so, at least initially, by the end of that time. If regression has not begun at the end of eight weeks, our experience has shown that there is little reason to continue therapy with the same hormone over a longer period of time.

Occasional instances of "no change" (where the disease remains stationary during the period of observation) were exceedingly difficult to evaluate. Thus, it is obvious that the present series will be "weighted" with patients who have had short, nonbeneficial courses of therapy as compared to those patients showing objective improvement who have had continuous uninterrupted therapy over a long period of time.

The schedule of treatment employed in the 133 patients under study is shown in table 1. The number of courses of treatment received by each patient is as follows: 79 patients received one course of treatment, 32 patients received two, 9 patients received three, 7 patients received four, and 5 patients received five.

The particular hormone chosen for use in each patient was related to her physiological age in reference to her menopause. Prior to the menopause (whether natural or induced by irradiation or oophorectomy) and for a five-year period thereafter, the initial steroid of choice was always an androgenic hormone. After this arbitrary period (five years postmenopausal), treatment with an estrogenic hormone appeared to be decidedly more useful. However, experience has indicated that estrogens in moderate therapeutic doses when given premenopausally or in the early postmenopausal period may actually prove harmful by accelerating the course of the disease. Younger patients who fail to respond to initial androgen therapy should be given a short period of respite to allow for a "withdrawal effect" (regression of tumor that may follow the cessation of hormone therapy). After this interval these patients may be allowed a very cautious trial with estrogens in a desperate attempt to alter the tempo of this progressive and devastating disease. In place of estrogens, the adrenal steroids or endocrine ablation by surgery may be considered as an adjunct to hormone therapy at this stage of the therapeutic regimen. Androgen therapy can be used effectively in both premenopausal and postmenopausal patients, as it does not depend upon physiological age. Older patients failing to respond to initial estrogen therapy should receive a secondary course of androgens.

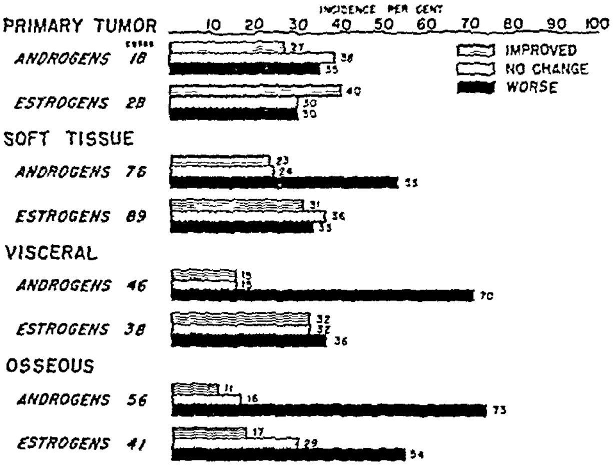

Fig. 1.—*Comparison of objective results of androgen and estrogen therapy.*

Results

Objective.—Results of therapy were compared in the following category of lesions: (1) primary, (2) soft tissue (including skin, subcutaneous tissue, and lymph nodes), (3) visceral (including pulmonary), and (4) osseous. The objective responses were recorded as improved, no change, and worse. The objective results of hormone treatment (with all treatment schedules combined and recorded as either androgen or estrogen) are shown in figure 1.

A critical evaluation of these results is difficult because of the variability in objective response as well as the inherent factor of the human equation in interpreting the findings. Patients showing definite objective improvement, even if it was followed by subsequent deterioration, were recorded as improved. On the other hand, patients whose disease appeared to remain static for a matter of months only to get worse ultimately under continuous treatment were recorded as worse. There were six such patients in the group receiving androgens and one patient in the group receiving estrogens whose disease showed no progress for periods of 2 to 10 months before advancement occurred.

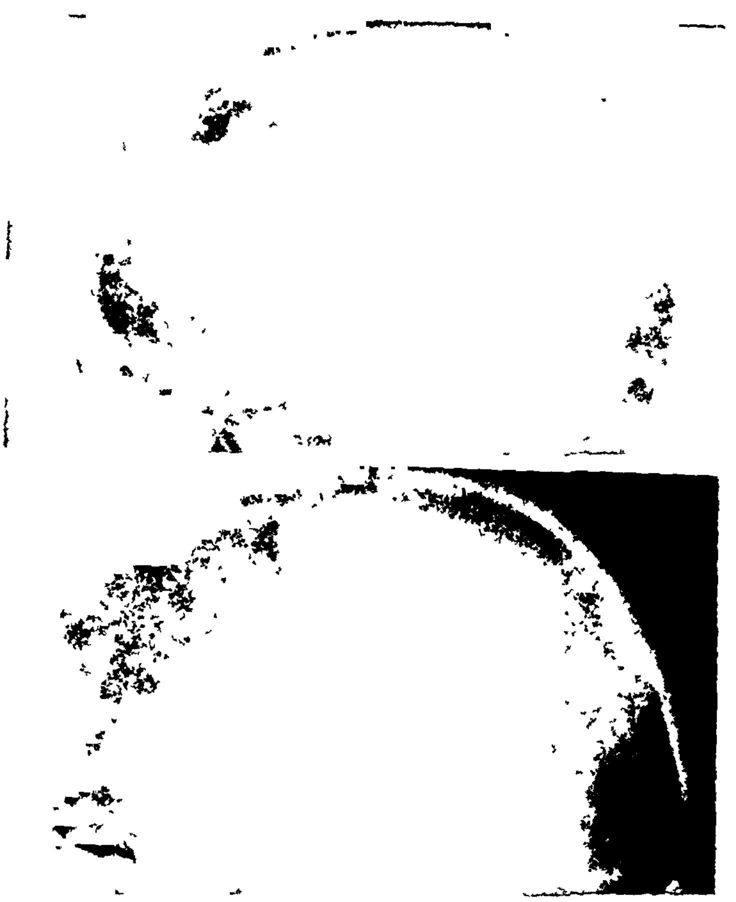

Fig. 2.—*Top,* large osteolytic skull metastases occurring while young woman was still receiving testosterone therapy. Multiple bone metastases developed after an initial favorable effect that lasted longer than one year *Bottom,* "withdrawal effect" shown by appearance of skull in same patient 6 months after discontinuation of testosterone therapy. No medicaments given during this time. Present remission has lasted longer than one year.

Evidence of a favorable objective response in the evaluation of osseous lesions requires both tumor regression and bone repair. This is usually characterized by the x-ray appearance of recalcification and increased density of osteolytic lesions, the re-formation of bone architecture and contour, and the healing of pathological fractures. These rather specific x-ray manifestations required for improvement may account for the relatively poor response shown by osseous lesions to hormone therapy. Occasionally, however, osteolytic bone lesions have been seen to undergo remarkable repair under hormone therapy, while new lesions develop or other osseous lesions progressed at the very same time. This paradox was observed in four patients under androgen therapy, and such results were reported as "worse" for the purpose of this study. Apparent acceleration of the disease occurred in two patients with osseous lesions. This required cessation of androgen therapy. Acceleration of the metastatic process has been observed in patients receiving both androgens and estrogens, but it is relatively uncommon except in premenopausal patients receiving estrogens

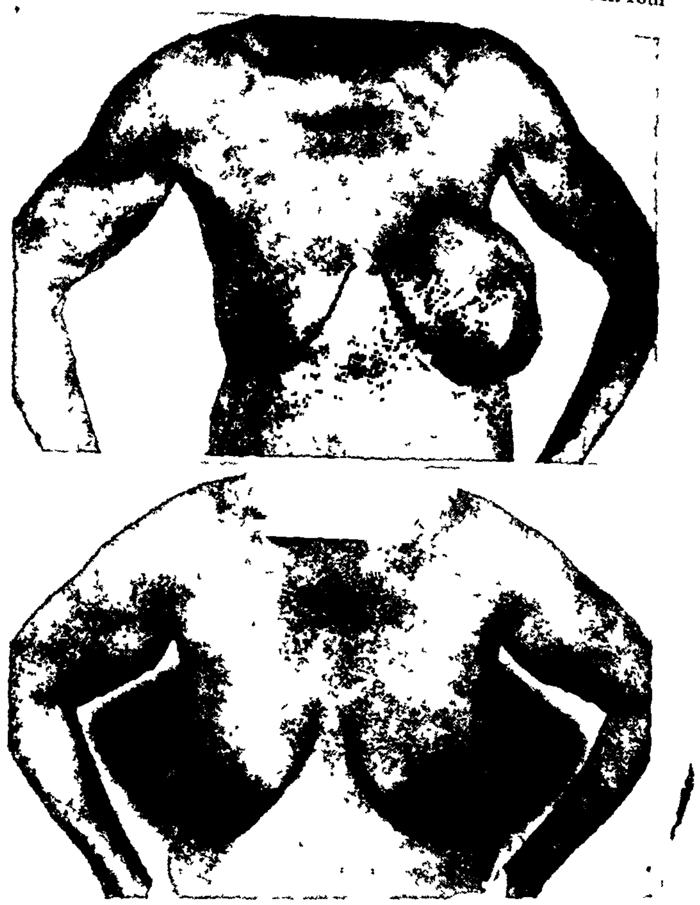

Fig. 3.—*Top,* large primary cancer of the left breast with axillary metastases. Patient considered "categorically" inoperable *Bottom,* appearance of primary tumor in same patient after 15 months of estrogen therapy. Marked regression of primary tumor and marked improvement in general appearance of patient.

TABLE 2.—*Subjective Results of Sex Hormone Therapy*

	Type of Therapy			
	Androgens (110 Cases)		Estrogens (100 Cases)	
Subjective Results	No	%	No	%
Well Being				
Improved	53	48	44	44
No change	27	25	37	37
Worse	30	27	19	19
Pain				
Complete relief	6	9	5	11
Partial relief	28	43	18	40
No change	8	12	3	6
Worse	23	36	19	43

In the palliative treatment of breast cancer one must give careful consideration to the well-recognized withdrawal effect of hormone therapy. Patients in whom the disease appears to reactivate while they are still receiving sex steroid therapy may show a marked improvement, with objective regression of the tumor, when treatment is discontinued. Huseby reported that 9 of 14 patients treated with estrogens "exhibited a second definite regression of their lesions lasting from 6 weeks to 9 months" when treatment was stopped. This phenomenon may even occur in patients who have failed to note a favorable initial response to therapy. In the present series, the favorable effects of withdrawal (of which there were several striking examples [fig. 2]) could not be included in the reported results for the obvious reason that these responses were not considered to be the direct consequence of treatment with either androgens or estrogens.

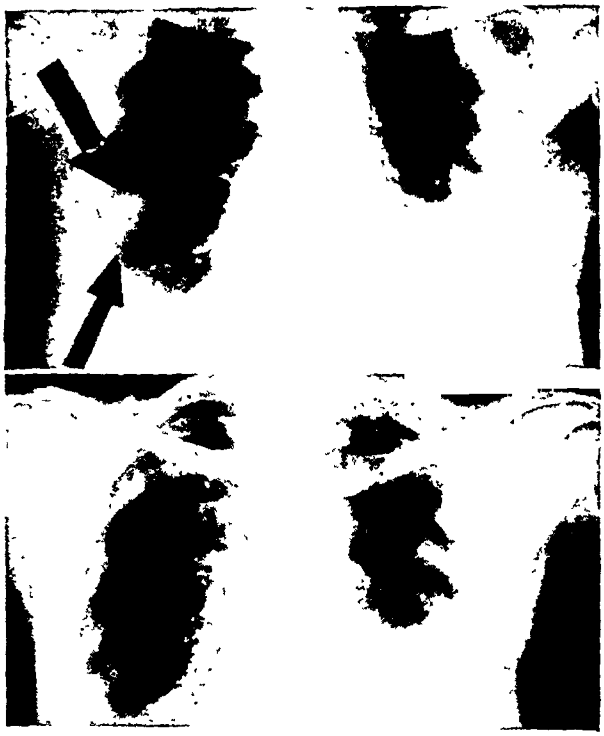

Fig. 4.—*Top*, large solitary lung metastasis in elderly woman. *Bottom*, disappearance of lung lesion after only 3 months of estrogen therapy. Patient ultimately died of liver metastases.

The results of this study (fig. 1) indicate that soft tissue and visceral lesions show a more favorable response in those patients receiving estrogens than in those receiving androgens. This superiority is considered statistically significant, as verified by the chi-square test ($p=0.05$). These conclusions are confirmed in general by the reported results of the Subcommittee on Steroids and Cancer.[10] The summary of their findings indicates that the "effectiveness of estrogen therapy for soft tissue and lung metastases increases with the age of the patient" and that in "women five years past the menopause estrogens are the hormones of choice for the treatment of soft tissue and lung metastases" (fig. 3 and 4).

In the present study, chlorotrianisene (TACE) appeared to be significantly less effective than either ethinyl estradiol or diethylstilbestrol in the treatment of visceral metastases. This finding has been confirmed by the Subcommittee on Steroids and Cancer, which found chlorotrianisene to be "unsatisfactory as an estrogenic mammary tumor-suppressant agent." Uterine bleeding was a very common complication of therapy with chlorotrianisene. In the present study there appeared to be no statistically significant difference between the several androgens used. (In the comprehensive studies of Segaloff and co-workers, the clinically effective androgens—testosterone, stanolone [Dihydrotestosterone], and methyltestosterone—share two distinctive properties: (1) they cause a decrease in the urinary gonadotropic hormone, and (2) they cause pronounced virilization.) The tumor-suppressing effect of these drugs showed no advantage over the accepted standard of reference, namely, the effect of testosterone propionate. Long-acting androgens such as testosterone cyclopentylpropionate involve certain inherent risks in the event of complications because their action cannot be interrupted promptly.

Subjective.—The subjective responses to hormone therapy were evaluated on the basis of well-being and relief of pain. These results are shown in table 2. Although a feeling of well-being was one of the most conspicuous benefits to be noted, in our experience there appeared to be very little difference in this euphoric effect between the androgens and the estrogens. However, it is well to be cautious in evaluating subjective improvement, as many steroids are known to produce a remarkable sense of well-being as a part of their anabolic effect. This can occur irrespective of the course of the disease and is particularly true with the androgens. All physicians are aware of the receptive mood of patients with incurable cancer. The power of hope in a patient with a hopeless disease is formidable; a mere placebo in a patient with advanced cancer may result in a remarkable subjective and spiritual improvement.

TABLE 3.—*Comparison of Objective and Subjective Results of Treatment with Stanolone and Testosterone Propionate*

	Results			
	Testosterone Propionate (62 Cases)		Stanolone (17 Cases)	
Objective and Subjective Responses	No.	%	No.	%
Objective				
Primary lesion				
Improved	2	25	...	...
No change	3	37.5	1	100
Worse	3	37.5	...	...
Soft tissue				
Improved	10	24	2	22
No change	12	28	3	33
Worse	20	48	4	44
Visceral				
Improved	4	20	2	29
No change	2	10	...	...
Worse	14	70	5	71
Bone				
Improved	4	13	1	11
No change	5	16	...	...
Worse	22	71	8	89
Subjective				
Well-being				
Improved	28	55	10	59
No change	17	33	4	24
Worse	6	12	3	17
Relief of pain				
Complete relief	4	10	1	8
Partial relief	13	33	9	75
No change	3	13	1	8
Worse	17	44	1	8

Relief of pain was a subjective response that seemed to be based upon a more tangible and well-defined effect. As Leriche has aptly said, the sensation of pain "is the resultant of the conflict between a stimulus and the whole individual." Pain usually occurred in patients who had osseous metastases, particularly to weight-bearing skeletal structures. As noted in table 2, complete or partial relief of pain occurred in 52% of the patients receiving androgens and in 51% of those receiving estrogens. However, in a small group of patients treated with stanolone, the complete and partial relief of pain appeared to be superior to that experienced with testosterone propionate (table 3), although the objective response in these two series was about the same.

Side-Effects

Although the usual side-effects of sex steroid therapy are quite well known, specific side-effects incident to intensive therapy often occur in the prolonged treatment of advanced mammary cancer with large and unphysiological doses of hormones. The incidence and degree of these side-effects are related to both the total dose and the duration of treatment, as well as to the individual sensitivity of the patient. The incidence of these characteristic side-effects of treatment is shown in figure 5.

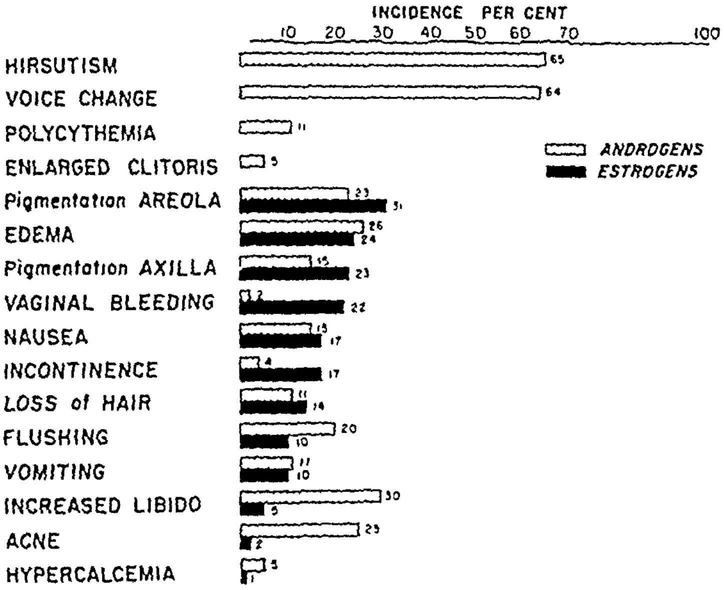

Fig. 5.—Incidence of side-effects of androgen and estrogen therapy.

Androgens.—The most prominent side-effects produced by androgen therapy were hirsutism and hoarseness, followed in frequency by increase in libido, edema, and acne. Hirsutism occurred in at least 65% of the patients treated with androgens and was most noticeable in brunette women with a natural predisposition toward excessive facial and body hair. From a cosmetic point of view this masculinizing side-effect was frequently very disturbing, particularly to younger patients. Voice changes, consisting primarily of hoarseness, occurred in 64% of those receiving androgens. This deepening of the voice is the result of hypertrophy of the vocal cords. After cessation of therapy, it often took many months before the voice returned to normal.

An increase in libido was noted in a least 30% of the patients treated with androgens. This probably represents a minimal incidence, inasmuch as many women were reticent about discussing so personal a problem. Kennedy and Nathanson,[11] in their excellent study of side-effects of sex steroids, confirm earlier findings that "androgens cause an increased susceptibility to psycho-sexual stimulation, enlargement of the clitoris and increased sensitivity of the external genitalia." Although the incidence of enlargement of the clitoris was only 5% in the present series, it must be noted that pelvic examinations were not performed routinely. Acne and a coarsening of the skin occurred in 25% of the patients receiving the androgens. This acneiform eruption varied from mild to severe, but occasionally it was pustular and cosmetically quite distressing. In those patients with severe acne, it appeared early in the course of treatment, often within the first few weeks.

Estrogens.—The most prominent side-effects produced by estrogen therapy were pigmentation of the areola and axilla, edema, and vaginal bleeding. Nausea, vomiting, and incontinence usually were disturbances of a secondary order of importance in both their incidence and their degree of discomfort.

Pigmentation of the areola and axilla was observed in 31 and 23%, respectively, of the patients treated with estrogens. Pigmentation of the areola is much less noticeable in Negro women. In contrast to the frequency of pigmentation of the areola and axilla, gross enlargement of the uninvolved breast was infrequent. Vaginal bleeding occurred in 22% of postmenopausal patients receiving estrogens. The uterine flow was usually minimal (consisting of staining or spotting), and therapy could often be continued without interruption. Occasionally, however, bleeding was sufficient to require curettage or modification of the prescribed dose. Withdrawal bleeding occurring 5 to 10 days after the cessation of therapy was noted particularly in elderly women. This usually lasted no longer than one to two weeks. Vaginal bleeding associated with androgen therapy was a rare occurrence but was present in 2% of the patients.

Urinary incontinence, usually of the stress type, occurred in 17% of the patients treated with estrogens. Although this sign was usually mild, it often proved embarrassing to elderly women. Nausea, occasionally associated with malaise, anorexia, and vomiting, was the commonest gastrointestinal side-effect observed. Administration of the hormone between meals, as well as a gradual increase in the dose schedule, usually permitted full tolerance of the drug despite these disagreeable effects.

Both androgens and estrogens are known to produce an increased retention of sodium and a corresponding increase in extracellular fluid. Edema was noted in 26% of the patients receiving androgens and in 24% of those receiving estrogens. However, there were many patients (particularly among those receiving testosterone) who gained 5 to 15 lb. (2.3 to 6.8 kg.) in weight without gross evidence of ankle edema. It is difficult but important to attempt to differentiate the water-retaining effect from the anabolic effect when evaluating weight gain in the patients treated with androgens. It is well known that an individual can gain up to 10 to 12 lb. (4.5 to 5.4 kg.) in edema fluid before clinical evidence becomes apparent. In the patient with a previously compromised cardiovascular system, this increase in extracellular fluid may precipitate or hasten decompensation.

Kennedy and Nathanson have reported that "in 17 patients (9 per cent) of those receiving estrogen therapy, fluid retention led to congestive cardiac failure or exaggerated an existing mild decompensation." Any additional cardiovascular strain in older patients may precipitate cardiac decompensation. Patients with known cardiac disease should be given hormones with great caution. Also, postmastectomy lymphedema can frequently be aggravated during hormone therapy. Although salt and fluid retention can be a serious complication of hormone therapy, particularly in patients with cardiovascular disease, simple measures may be undertaken to minimize this contingency. A low-salt diet and rigid fluid restriction in addition to diuretics and digitalis when indicated may allow patients to continue hormone therapy without interruption.

Table 4.—*Comparison of Side-Effects of Ethinyl Estradiol and Chlorotrianisene (TACE)*

	Ethinyl Estradiol (50 Cases)		Chlorotrianisene (41 Cases)	
Side-Effect	No	%	No.	%
Edema	10	20	9	22
Bleeding	5	10	13	32
Flushing	4	8	4	10
Nausea	6	12	10	24
Vomiting	3	6	4	10
Loss of hair	7	14	5	12
Pigmentation of areola	22	44	9	22
Pigmentation of axilla	14	28	4	10
Incontinence	7	14	6	15

Hypercalcemia is an infrequent but serious side-effect, occurring in 5% of the patients receiving androgens and in 1% of those receiving estrogens in the present series. However, it has been reported more frequently by the Committee on Research, occurring in 7.7% of patients treated with estrogens and in 14.2% of those treated with androgens. Clinical evidence of hypercalcemia is manifested by anorexia, nausea, vomiting, and weakness, which in severe cases may go on to disorientation, stupor, and coma. Initial symptoms may be deceptively mild, but the syndrome may progress rapidly to a hypercalcemic crisis, renal failure, and death. The syndrome of hypercalcemia may be difficult to rectify, but immediate cessation of therapy is always mandatory. Supportive therapy, consisting of a low-calcium diet and infusions of saline solution, dextrose, and a 2.5% solution of sodium citrate, often proves helpful. Pearson, West, and Hollander [12] have reported that cortisone has been used very successfully in several cases of hypercalcemia. The effectiveness of this drug has been amply confirmed by others. The subsidence of hypercalcemia and hypercalciuria was associated with prompt clinical improvement.

Laszlo and his co-workers [13] have studied the mineral metabolism of patients with bone metastases and have not infrequently found elevated levels of urinary calcium and phosphorus excretion even without hormone treatment. When the amount of calcium created by osteolysis due to tumor invasion exceeds the amount that the kidney can excrete, hypercalcemia results. Thus, hypercalcemia may occur spontaneously in patients with osseous metastases as well as in those with the more serious hormone-induced syndrome. In the current study, hypercalcemia was defined as any calcium level in excess of 12 mg. per 100 cc. of blood. None of the patients in the present series who showed evidence of elevated blood calcium levels had clinical symptoms of hypercalcemia. Perhaps the low incidence of serious hypercalcemia can be attributed to the predominance of ambulatory patients such as are seen in a clinic. In bedridden patients with metastases who are immobilized over a long period of time, osteoporosis and disuse may excessively elevate the calcium level.

Comparison of the various estrogens and androgens used in this study failed to reveal any striking difference in the incidence of their side-effects. However, in the specific comparison of side-effects caused by ethinyl estradiol and chlorotrianisene, some significant differences are shown in table 4. A statistically valid variation occurred in the frequency of vaginal bleeding (10% for ethinyl estradiol as compared with 32% for chlorotrianisene) and in the incidence of pigmentation changes. The side-effects of stanolone when compared with those of testosterone showed all of the predominant androgenic characteristics except a lower incidence of increased libido. The number of patients showing side-effects due to combined estrogen-androgen therapy was not sufficient for critical evaluation. However, the specific changes caused by individual sex steroids may be masked or minimized by combined treatment.

Table 5.—*Results of Combined Androgen-Estrogen Therapy*

	Results (8 Patients)	
Type of Lesion and Classification of Response	No.	%
Objective response		
Primary		
Improved	...	...
No change	2	67
Worse	1	33
Soft tissue		
Improved	1	17
No change	1	17
Worse	2	66
Visceral		
Improved	1	20
No change	3	60
Worse	1	20
Osseous		
Improved	...	...
No change	1	25
Worse	3	75
Subjective Response		
Well-being		
Improved	4	50
No change	2	25
Worse	2	25
Relief of pain		
Improved	3	50
No change	2	33
Worse	1	17

Combined Androgen-Estrogen Therapy

There were eight patients who received complete courses of ethinyl estradiol (3 mg. daily) plus testosterone propionate (100 mg. three times weekly) simultaneously. The results of this combined treatment are shown in table 5. A critical analysis of this small sample is, of course, unwarranted, but there would appear to be no striking superiority in either the objective or subjective response over that of similar treatment with either hormone alone.

Survival

Although there is little doubt that the sex steroids are effective in the palliative treatment of advanced cancer of the breast, it would be of equal importance to know whether this type of therapy actually prolongs survival time. However, the unequivocal answer to this problem remains to be solved. One must be extremely cautious in selecting "comparable series" for this type of a statistical study, as it is readily apparent that the degree of advancement of the disease is difficult to determine and the heterogeneous composition of these preterminal groups is so conspicuous. Despite this question of validity of comparison among dissimilar series, the Committee on Research states that steroid therapy "may prolong life" as demonstrated by the following figures taken from their Second Conference on Steroids and Cancer[10]: 347 patients with soft-tissue involvement were treated. The average survival rate for the patients whose conditions were not improved was 7.5 months, while, for the 100 patients who showed tumor regression for an average period of 6.1 months, the survival rate averaged 13.57 months. Thus, patients who responded to treatment lived twice as long as those who failed to respond.

Hallberg, Nohrman, and Sylven[14] compared the mean survival time in two series of patients, taking time zero as the date of diagnosis of bone metastases. Patients with visceral lesions were excluded from the study, but patients with soft-tissue metastases were included. One series of 97 patients was treated with testosterone alone, and a control series of 254 similar patients was treated by palliative radiotherapy. The mean survival time for the patients treated with androgens was 21 months, as compared with 15 months for the controls. Hallberg, Nohrman, and Sylven conclude that "the data suggest that androgen treatment significantly increases the length of survival."

Huseby[15] has recently presented a comparison in longevity between a group of 58 patients in Minnesota with "generalized" metastases treated with estrogens from 1946 to 1951 and a seemingly similar group of 193 patients in California treated palliatively (without hormones) by Shimkin and his colleagues from 1918 to 1947.[16] The mean and median survival times were 10 and 7.8 months, respectively, for Shimkin's group and 20.3 and 16 months, respectively, for Huseby's group. Huseby found by analysis that the difference in survival time between patients in these two series was statistically highly significant.

Thirty-one patients in the present series with advanced disease were treated with the sex steroids only from the time of diagnosis until death or until they were lost to further follow-up. Also, seven of these patients are still alive and are receiving treatment at the present time. Results of a life table were found to be difficult to evaluate critically because of the small number of patients in the study and the large number of withdrawals. Those patients withdrawn from observation tend to increase the uncertainty of the estimate (and therefore increase the standard error). However, the three-year survival from the time of diagnosis of advanced or metastatic breast cancer was 24%, with a very large standard error of ± 18.6%. It is hoped that homogeneous series similarly treated (with and without hormones) will be reported by other investigators so that survivorship and prolongation of life may be more accurately compared. It is to be noted that a statistically valid conclusion as to whether life is lengthened in these patients treated with hormones can be made only when their survival is compared with that of a group of completely untreated patients. However, in this age of modern surgery, radiotherapy, castration, adrenocorticoid therapy, and other chemotherapeutic adjuvants, it is doubtful that such a series of untreated cases will ever again be found. Older series were found to be deficient in several respects, thus invalidating comparison.

Comment

It is to be pointed out that the individual groups of patients receiving androgen and estrogen therapy were not entirely comparable by virtue of some difference in their age range. Androgen therapy was used in both premenopausal and postmenopausal patients, whereas estrogen therapy was used only in postmenopausal patients. Despite some conflict in the medical literature,[17] cancer of the breast in young premenopausal women appears to be a more menacing disease. Therefore, one may be permitted to question the validity of the relatively poor results of androgen therapy in a group of younger premenopausal women in whom the prognosis is known to be less favorable. Present experience confirms the well-known fact that the relentless growth of mammary cancer can be modified and even caused to regress by appropriate alterations in the hormonal environment. However, despite even the most spectacular remission after a change in the endocrine milieu, the disease ultimately progresses by adapting itself to its new environment. Thus, since hormone therapy for advanced mammary cancer is time-limited and unpredictable in its palliative effectiveness, it should be used only after more definitive measures of treatment such as surgery and radiotherapy are no longer applicable. The duration of objective remission under hormone therapy was highly variable in point of time, lasting from a few months to an indefinite period of years. In the exceptional instances of long-lasting benefit, we tend to celebrate our successes without proper regard for the degree of host resistance—an unknown factor of the utmost importance.

In addition to sex steroid therapy, a variety of endocrine procedures designed to alter the hormonal environment have been known to induce a temporary remission in patients with advanced mammary cancer. Such operations for endocrine ablation as oophorectomy, adrenalectomy, and hypophysectomy have been used beneficially in the palliative treatment of this disease. Cortisone and its derivatives, with or without thyroid medication,[18] have been used with some success, particularly in patients with metastases to the brain. However, it is not the purpose of this paper to review these several modalities of endocrine ablation or to discuss their role in the total treatment of this disease. Whereas interruption of ovarian function is most successful in young women with advanced mammary cancer and the administration of the estrogens is of greatest benefit in elderly women, in androgen therapy the age of the patient appears to be of relatively little importance. A notable effort is being made in biochemical research to discover newer sex steroids that, on the one hand, will have an even greater potency of tumor suppression and, on the other, will have an even lower incidence of undesirable side-effects. Thus far, however, there appears to be no androgen possessing positive superiority over testosterone and no estrogen to excel either ethinyl estradiol or diethylstilbestrol. The degree of response to therapeutic doses as compared to massive doses of the same drug remains to be clarified.

Summary and Conclusions

One hundred thirty-three patients received 223 complete courses of sex hormone therapy for advanced mammary cancer. The choice between estrogen and androgen was made principally in relation to the physiological age of the patient in reference to her menopause. Estrogens were used only after five years had passed since the menopause, whereas androgens were found to be useful in both premenopausal and postmenopausal patients. However, in the definitely older patients, estrogen appeared to be the hormone of choice.

A favorable objective response occurred with estrogen therapy in 40% of patients with primary tumors, 31% with soft-tissue lesions, 32% with visceral lesions, and only 17% with osseous lesions. Both stilbestrol and ethinyl estradiol were found to be superior to chlorotrianisene (TACE) in estrogen therapy. A favorable objective response occurred with androgens in 27% of patients with primary tumors, 23% with soft-tissue lesions, 15% with visceral lesions, and only 11% with osseous lesions. There appeared to be no significant difference in objective therapeutic effectiveness between the several androgens used. The optimum dose of testosterone propionate was 50 to 100 mg., given intramuscularly three times weekly. Complete or partial relief of pain occurred in 52% of the patients treated with androgens and in 51% of those treated with estrogens. Stanolone appeared to be superior to testosterone propionate in the subjective relief of pain. A sense of well-being occurred in 48% of the patients treated with androgens and in 44% of those treated with estrogens.

Although the sex hormones are certainly not a "cure" for advanced mammary cancer, in the total care of this disease they do offer profound and gratifying benefits for patients beyond the scope of surgery and radiotherapy. Whereas "severity is allowable when gentleness is in vain," it has been our practice to make full use of the initial palliative benefits of hormone therapy before considering the more drastic operative procedures such as adrenalectomy or hypophysectomy.

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Acne Vulgaris.—The main aim of therapy in acne vulgaris is to remove the blockage from the mouth of the pilosebaceous follicles, thereby allowing the retained sebum to escape on to the surface of the skin, and to decrease the size and activity of the sebaceous glands. This aim could be realized quite simply by giving suitable amounts of estrogens, were it not that the dose necessary would cause feminization in males and uterine bleeding in females. To a certain extent, however, it is possible to produce similar results by different means. . . . Soap and water attain therapeutic qualities in local treatment, especially when the skin is greasy and comedones are plentiful. The face should be washed four or five times a day in hot water and then briskly rubbed with a soft towel. The exact type of soap is unimportant, but the addition of borax or sodium bicarbonate to the water is helpful. Sulphur is the most useful local application, as it causes an exfoliation of the surface layers of the epidermis, thus removing the comedones. To maintain a mild peeling of the skin should therefore be the aim of treatment. The sulphur can be incorporated in a lotion, emulsion or paste. Care must be taken not to cause too drastic a reaction and this is especially likely to occur in fair-skinned individuals. Two or four per cent of sulphur is a reasonable strength with which to begin and this may be slowly increased up to ten or twelve per cent.—P. F. Borrie, M.D., M.R.C.P., Acne Vulgaris, *The Practitioner*, May, 1956.

SORTING—THE KEY TO MANAGEMENT OF VICTIMS OF DISASTER

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• *The simultaneous infliction of injuries of all degrees on a large population must be anticipated in the event of either natural or nuclear disasters. When facilities for treatment are limited, the greatest possible number of lives can be saved only by making sure that these facilities are not exhausted by injudicious use on either the trivial or the hopeless cases. Triage, the sorting of the injured, must be done by the most mature surgeon available. It decides questions of treatment, of transportation, and of return to duty. Its effectiveness is enhanced by attention to the changing tactical situation. The principles of triage here stated were developed under conditions of conventional warfare. But it must be assumed that with certain modifications they will apply also under the altered conditions of the future, such as the sudden outbreak of nuclear warfare or the occurrence of natural disasters in a more densely populated world.*

The medical management of large numbers of sick or injured, whether they result from epidemic disease, combat, or disaster, involves the establishment of an organization that takes into consideration every essential of proper care. This orderly process of medical management insures that wherever possible each patient will receive treatment in proportion to his degree of morbidity and disability and under no circumstances will the lives of the many be jeopardized by the medical needs of the one or of the few. In order to function properly, this organization must be prepared to classify and categorize its patients on the basis of type and severity of wound or disease condition so that a minimal time loss in the institution of proper therapy and disposition of each case can be expected. Early classification permits visualization of over-all medical requirements for large groups of casualties and, on this basis, aids in the decision as to when, where, and what type of therapy should be instituted. Lack of early classification of the sick and wounded en masse leads to confusion, chaos, and increased mortality, for then each patient is individually treated without regard for the more urgent needs of others in the group or for the medical capabilities of the organization.

Sorting, or triage, is officially defined by the U. S. Army as the procedure by means of which the sick and wounded are classified according to type and urgency of condition presented, so that they can be properly routed to medical installations appropriately situated and equipped for their care. It is a procedure that had its inception in the care of those wounded in combat but that, with only minor modification of specific detail, may be equally as well applied to any organization having as its responsibility the care of large numbers of injured generated relatively simultaneously. Sorting is, in fact, the key to the management of these patients, for it is only by its means that casualties may be categorized properly and separated so that there will be a minimal time lag between injury and the onset of therapy. In its application, sorting considers the necessity for overlooking no one and for doing the greatest good for the largest number of casualties. Both these goals are accomplished by taking into consideration the medical capabilities of the installations involved and the relative proportion between the number of professional personnel available for the institution of therapy and the total number of patients requiring treatment.

Decisive Factors in Sorting

Sorting is directed toward making decisions with regard to, first, the establishment of criteria for the return of the injured to duty. In combat, this decision will vary with both the type of wound sustained and the specific tactical situation, so that under no circumstance will a casualty be returned to duty if his incapacitation might interfere with the conduct of the battle. Conversely, no casualty will be unduly delayed in his return to duty, for delay would result in the need for a replacement, and it is uneconomical to replace a battle-tried veteran with an unseasoned soldier. It thus becomes necessary to hold and treat casualties for periods of time that vary according to type and severity of wound, for upon return to duty these casualties must be assets rather than liabilities to their organization. In this way, a priority for return to duty is established by weighing clinical condition against tactical requirements. In a disaster, on the other hand, clinical condition must be weighed against manpower shortages. Thus, the size of the disaster and the availability of outside help for the institution of rescue and of first-aid and emergency medical treatment may determine what type of injured, and how many, must be released in order to aid in the care of the other victims. Early release of disaster victims may also be determined on the basis of available hospitalization facilities, so that overcrowding and consequent jeopardy to health may be minimized.

The second decision to be arrived at in sorting concerns the establishment of priority for treatment. Because the type and urgency of the therapy to be employed will vary with the severity of the wound, a priority must be established for the care of the various types of wounded. Treatment priorities are not only dependent on the urgency of therapy required but also vary with the stated function of a particular installation, for it is on this basis that specially trained medical personnel are assigned and supplies and equipment allocated. Thus, the treatment to be given must be within the medical capabilities of the particular installation. With an adequate number and type of assigned professional personnel, priorities for treatment may have to be varied by the type and availability of medical supplies and equipment. Typi-

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cally, a hospital with only a limited supply of blood on hand and with little likelihood of more becoming available in the near future will spread the use of that blood so as to aid in the recovery of the largest number of injured. On this basis, the critically wounded man who would require all of the only 10 units of blood available in order to aid in his possible recovery would drop in priority to a position below that of the five casualties whose certain recovery would be insured by the receipt of 2 units each. Conversely, where only 2 units of blood are on hand to treat the shock of 10 casualties, the best utilization of this item would entail using it in the resuscitation of no more than 1 or 2 of these casualties rather than wasting it by giving each only 1/5 unit.

Establishment of priority for treatment may also be varied by the number and caliber of physicians available for the institution of treatment. Thus, in a disaster zone in which all physicians have become disabled and the institution of therapy must be accomplished by ancillary medical personnel, such as dentists, veterinarians, and nurses, little would be accomplished by the establishment of priorities for surgical procedures of other than minor magnitude, for they would be beyond the capabilities of the available personnel. In such a situation, only priorities for resuscitation and emergency medical treatment would be instituted. These casualties would then be evacuated to other installations whose personnel are more capable of handling the complicated technical surgical procedures required. Where large supplies of medical matériel are immediately available, in an installation adequately staffed for the care of any casualty, the priority for surgical treatment will depend on the type and urgency of treatment required.

The third type of decision to be rendered is the casualty's need to be evacuated for further treatment and the timing of this move in relation to the program of therapy. Basically, requirements for evacuation are determined by the need to conform to the tactical situation, which limits the number of noncombat personnel and matériel brought into a combat zone. This limitation is necessary to prevent excessive interference with the mobility and maneuvering of the tactical force and allows for only a few small, highly mobile medical installations in the area. The evacuation of casualties either to prevent their interfering with the conduct of the battle or in order to insure them more adequate treatment in the larger, less mobile, better-equipped installations farther to the rear is, therefore, necessary. Obviously, evacuation should be performed only for those casualties whose physical deterioration will not be accelerated by it and should be carried out in such a manner that safeguards will be provided against such an eventuality. Thus, a system of priorities for evacuation is established in the determination of which physical condition is weighed against the rigors of travel and both are balanced against the available means for transportation.

Although in some instances the priority for evacuation is the same as the priority for treatment, frequently the necessity for early urgent therapy is of such a high degree that unwise early evacuation prior to treatment could result in death. For example, a casualty in severe shock as the result of uncontrolled bleeding from a laceration of the femoral artery enjoys a high priority for the control of his bleeding and the treatment of shock and no priority for evacuation. After necessary resuscitation has been performed, he then receives a high priority for evacuation so that vascular surgery may be performed early. Each surgeon, as he sorts to determine priority for evacuation, must assess the urgency and degree of essential medical care against the available means of evacuation and the supporting medical capabilities. He must avoid arbitrary sorting for evacuation by determining that there is a place to which casualties can be evacuated, that there are suitable means for evacuation, and that the patient is in a fit state for this evacuation. All these factors will vary with the particular situation, and sorting must, under all conditions, be permitted to remain flexible.

Other Considerations

All sorting, since it requires a high degree of professional skill in making the requisite clinical judgments, should be performed by the most mature surgeon of a given installation. These decisions are based on clinical experience plus an expert knowledge not only of the particular tactical situation but also of the medical capabilities of all installations in the treatment chain. A realistic appraisal must be made regarding the likelihood of survival, the time required to perform the needed technical procedures, and the capabilities for medical care available at the time and place. Errors in judgment will lead to increases in morbidity and mortality through submitting to surgery casualties who have not been adequately resuscitated, evacuating injured without regard to clinical condition or the rigors of movement, and attempting procedures beyond the capabilities of the installation.

Sorting is a continuous procedure that starts with initial medical care and terminates only with the final disposition of each patient. It must establish priorities at each installation in the treatment chain because the function, medical capabilities, and facilities of each are different, and due consideration, in the light of these factors, must be given to every casualty upon his arrival in the installation. Moreover, the condition of the patient will change as a result of the institution of resuscitative treatment, necessitating re-sorting. Furthermore, a continuing influx of casualties may cause a change in the priority for treatment and evacuation of the injured already present. These changes produce the need not only for sorting at each installation but also for a revision of priorities at fairly frequent intervals in each.

In addition to all of the foregoing factors, or perhaps because of them, sorting is necessarily a flexible procedure, for the considerations influencing the required decisions will vary from day to day and from one situation to another. Typically, the surgeon who sorts by rote may fail to consider many factors important in making the proper decisions. For example, he might overlook the fact that a disparity between the number of wounded and the total number of personnel available for institution of therapy might require a larger number of early evacuations to less crowded installations. If he fails to consider the need to move his installation in keeping with the tide of battle, he may accept more casualties than he can treat in the time allotted prior to the move. If, in his sorting for evacuation, he fails to consider inclement weather as a deterrent to helicopter travel, he may bring about increased mortality by subjecting casualties to traumatic overland ambulance hauls. The ever-changing tactical situation must be observed and sorting remain flexible and subject to modification as needed.

As enunciated in the preceding paragraphs, sorting has as its objective the classification and separation of large numbers of sick and wounded so that priorities for treatment, evacuation, and return to duty may be more easily established. This system has evolved by trial and error through past wars until at the present time we pride ourselves on the fact that by its means no casualty is ever denied treatment. Treatment is usually commensurate with the severity of injury and the quality and number of facilities and personnel available; the time lag between wounding and the institution of therapy is reduced to a minimum; and, because of its efficiency, we accomplish the greatest good for the largest number. Remember, however, that this concept of the establishment of priorities was developed during conventional warfare and was based on an unfailing source of medical supplies and little or no disproportion between numbers of casualties and quantity and quality of medical personnel available for treatment. In practice, this system has resulted in priorities for treatment usually being established on the basis of wound severity, so that the most severely wounded enjoy the highest and the least severely wounded the lowest priority.

Priority System for Nuclear Warfare

Prior planning for the surgical care of mass casualties resulting from nuclear warfare, where limited treatment facilities, inadequate supplies, and a shortage of medical personnel will prevail, makes it evident that, in order to provide no disservice to the many in favor of the few, some modification of our priority system must be established. Such a modification, as outlined in a Department of the Army technical bulletin[1] provides, in the event of atomic disaster, for all injured to be divided into four groups:

1. Casualties requiring minimal treatment:
   a. Those who may return to duty after minimal treatment is given.
      (1) Those with small lacerations or contusions.
      (2) Those with simple fractures of small bones.
      (3) Those with second degree burns of less than 10% of body surface and not involving incapacitating burns of face or hands.
   b. Noneffectives who require domiciliary or nursing care after minimal treatment is given.
      (1) Those with disabling minor fractures.
      (2) Those with burns of the face or hands of less than 10% extent but which interfere with the individual's ability to care for or feed himself.
      (3) Those with moderate neuropsychiatric disorders.
2. Casualties requiring immediate care:
   a. Those with hemorrhage from an easily accessible site.
   b. Those with rapidly correctable mechanical respiratory defects.
   c. Those with severe crushing wounds of the extremities.
   d. Those with incomplete amputations.
   e. Those with severe lacerations involving open fractures of major bones.
3. Casualties whose surgical treatment may be delayed without immediate jeopardy to life:
   a. Those with closed fractures of major bones.
   b. Those with moderate lacerations without extensive bleeding.
   c. Those with second degree burns of less than 30% and third degree burns of less than 20% of the body surface.
   d. Those with noncritical central nervous system injuries.
4. Casualties whose therapy will be expectant:
   a. Those with critical injuries of the central nervous system or respiratory system.
   b. Those with significant penetrating or perforating abdominal wounds.
   c. Those with multiple severe injuries critical in nature.
   d. Those with severe burns of large areas (second or third degree burns of 40% or more of the body surface).

It is estimated that in atomic disaster group 1, those requiring minimal treatment, will comprise approximately 40% of the total casualties. These casualties truly have no priority for treatment but in practice will receive their treatment early. Ordinarily, their wounds are of such a nature that the treatment they receive while being sorted is all the therapy that they require, and they can then be returned to duty or remanded to domiciliary care.

Group 2, those requiring immediate care, is expected to comprise 20% of the total number of casualties. These injured will enjoy the highest priority for surgical treatment because a relatively short procedure will suffice to save life. Further, more definitive surgery for these casualties can then be delayed, although the possibility of infection must be accepted as the price of this delay.

Group 3 is expected to comprise 20% of the total and is composed of casualties a delay in whose surgical treatment will probably lead to infection but whose lives will not be jeopardized by the delay. The time lag between wounding and surgery for this group will be dependent on the total number of casualties of all types and the number of professional personnel available to institute surgical treatment.

Group 4 is expected to comprise 20% of all casualties resulting from the explosion of a nuclear weapon. Their expectant treatment will not be one of masterful neglect but instead will consist of that resuscitation and emergency medical treatment that the available facilities, total supplies, and number of professional personnel permits. Theirs will, however, be the lowest priority for treatment, because both the operative procedures and the resuscitative measures required are lengthy and technically complicated, so that the institution of therapy for one of these casualties would theoretically jeopardize the lives of several casualties in other priority groups. Increased loss of life in this group is accepted as a necessary consequence of this low priority for surgery.

Summary

Sorting is the key to the management of large numbers of injured generated during conventional comba for it is only through its utilization that modern pri ciples and practices of therapy may be proportionate applied to the combat wounded. Provided the enumerated changes in priorities are established, it will also become the key to the care of the larger number of simultaneously generated casualties resulting from the use of nuclear weapons in warfare. In civilian disasters or epidemics, adherence to the principles of sorting, establishment of priorities, and, where applicable, the need for evacuation will aid in minimizing morbidity and mortality.

Sorting is the procedure by means of which the sick and wounded are classified according to type and urgency of condition presented, so that they can be properly routed to medical installations appropriately situated and equipped for their care. It is a continuous procedure throughout the treatment chain and is practiced in each installation by the most mature surgeon available. The effectiveness of sorting is enhanced by observation of variations in the tactical situation. Sorting is directed toward establishing criteria for return to duty and priorities for treatment and evacuation. With certain changes in priorities, sorting as practiced during conventional warfare may be applied as the key to the management of casualties caused by either natural or nuclear disasters.

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THE DETERMINATION AND CLINICAL VALUE OF UROPEPSINOGEN

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- *Determination of the concentration of pepsinogen in the urine can be technically practical and clinically useful. It may offer a better index of gastric peptic activity than does intubation, and it has been useful in the differential diagnosis of peptic ulcer versus gastric carcinoma. Uropepsinogen values can aid in locating the site of hematemesis and can assist in the diagnosis of pernicious anemia. The response of uropepsinogen to hormone stimulation may provide many diagnostic, as well as therapeutic, indexes to endocrinological conditions.*

Although 49 papers dealing with the subject of pepsinogen in the urine have been published since Bucher's[1] comprehensive review in 1947, there still exists a controversy as to its clinical usefulness. Much of the debate, so well described by Bridgewater,[2] is due to criticism of methodology rather than of clinical results. Most of the adverse criticism comes from those who employ the Anson and Mirsky tyrosine method[3] of determining the quantitative concentration of uropepsin in the urine. This procedure is cumbersome. It is full of potential pitfalls, is expensive, and requires a highly trained technician if the results are to be relied upon. In contradistinction, those who have utilized the simpler method herein presented have in the main concurred with us that the determination is both technically practical and clinically useful. The patient may follow his usual routine, no fasting or withholding of medication being necessary. Since, as Spiro[4] has indicated, uropepsinogen values may offer a better index of gastric peptic activity than those analyses in which gastric intubation is routinely required, their determination has considerable clinical promise. Furthermore, the simplified method employed is applicable in those hospitals not equipped to carry out highly technical procedures.

Many authors have recognized the value of uropepsinogen in considering differential diagnoses.[5] It has proved useful in the diagnosis of gastrointestinal disease, notably peptic ulcer and gastric carcinoma. In macrocytic anemias, associated with an achlorhydria not altered by stimulation with histamine, it is a reliable differential test in excluding pernicious anemia.[6] In cases of massive hematemesis, uropepsinogen values have been useful in the consideration of the differential diagnoses. Low levels have been consistently found in bleeding esophageal varices, whereas in cases of bleeding duodenal ulcers the values are consistently high. Early in the hospital course when gastric analysis may not be feasible, a simple quantitative test of the urine for uropepsinogen may be of critical value.

An apparent relationship between the level of uropepsinogen and the state of activity of the adrenal cortex has been noted.[7] In Gray's study[5a] "there was noted a marked diminution in excretion [of uropepsinogen] in patients with panhypopituitarism and Addison's disease and a definite increase in the excretion in patients with Cushing's disease, accompanied by parallel alterations in corticoid and ketosteroid excretion." Replacement therapy in both groups was manifest in the uropepsinogen's stabilization at normal concentrations. It has been postulated that the uropepsinogen response to hormone stimulation may be an index of gastric hypersecretion in patients undergoing prolonged treatment with cortisone or corticotropin. The presence of a high output might herald impending complications of hormone therapy, notably, the development of a duodenal ulcer, hemorrhage, or perforation. Boland[8] has demonstrated that this aspect is becoming increasingly important in this steroid era. Thorn[9] and others[10] have verified the work of Garst

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and Hilliard [11] demonstrating the relationship between uropeptic activity and the state of the pituitary-adrenal axis. The clinical practicality of a simple determination of the concentration of uropepsinogen in a specimen of urine is apparent.

Physiological Considerations

Mirsky and his co-workers [12] verified the work of earlier investigators by establishing two facts: The source of uropepsinogen is the stomach, and it reaches the urine in some other way than by resorption from the intestine. If this be true, then an animal that had undergone total gastrectomy would have no pepsinogen in the urine. This has been shown repeatedly to be true in a variety of animals and in man. It was also concluded that since pepsin is inactivated at a pH of 4 and since blood is of a pH range 7.35-7.45, the pepsin-like substance in the urine must indeed be its precursor or zymogen—pepsinogen. Pepsinogen is stable at the pH of blood.

TABLE 1.—*Uropepsinogen Values in Normal Subjects and in Patients with Duodenal Ulcer*

Type of Subject	No. of Subjects	Uropepsinogen (Range), Mcg./Hr.	Uropepsinogen (Mean), Mcg./Hr.
Normal*	19	20.5—188.7	77.5
Duodenal ulcer	13	115.4—967.5	328.0

* Technicians and doctors on the laboratory staff with no symptoms of hematological, gastroenterological, or endocrine disorder.

These experiments indicate that the peptic gland is both an exocrine and endocrine organ. Janowitz and Hollander [13] have found a definite relationship between the exocrine and endocrine function as regards pepsinogen, this relationship being 99:1 (exocrine to endocrine). These results offer a sound basis for the consideration of the utility of a test for uropepsinogen in the detection of gastric peptic activity.

Experimental Procedure

Urine samples are collected in bottles containing 0.5 cc. of sulfuric acid (25%) to insure constant acidity. Pepsinogen in the urine is converted to pepsin by incubating a portion of the sample for one hour at 37 C with 2 *N* hydrochloric acid. A pH of 2.5 to 3.0 is necessary to obtain conversion. Buffered casein solution is added to an aliquot of the activated urine and the time required for the pepsin to flocculate casein particles is observed. This is the Goodman modification [6a] of the original West method [7a] referred to above as the "simpler" technique.

TABLE 2.—*Effect of Surgery on Uropepsinogen Values*

Reason for Operation	No. of Subjects	Mean Uropepsinogen, Mcg./Hr. Preoperative	Mean Uropepsinogen, Mcg./Hr. Postoperative	Type of Surgery
Duodenal ulcer	1	261.9	305.1	Vagotomy
Lesser curvature gastric ulcer	1	37 8	13.5	Subtotal gastric resection

Since the uropepsin assay is based upon comparison with crystalline pepsin, it was decided to express results in terms of micrograms of pepsin rather than arbitrarily defined units. Dilute solutions containing 0.05-0.30 mcg. of crystallized pepsin per 0.1 ml. are treated in the same manner with water, buffer, and substrate as the activated urine. The stock solution of pepsin (25.0 mg. in 250 ml. of dilute hydrochloric acid) keeps at least two months when refrigerated. The values for the pepsin solutions are plotted on log-log graph paper, and the urine values are calculated from it. The amount of pepsin per aliquot of activated urine is converted to micrograms per milliliter of urine. This figure is then multiplied by the total volume of the specimen divided by the four hours of collection, thusly: mcg. per ml. × vol./4 = mcg. per hour. Results obtained by two different technicians agree within 0.01 to 0.07 mcg. per 0.1 ml. (In order to facilitate comparison of our results with those of authors who have employed the arbitrary West "units," the reader may divide the micrograms per hour by 2.7). Each technician should construct his own standard curve daily in order to eliminate possible variations in the detection of the end-point by different technicians and to eliminate possible variations in different casein substrates. This is much the same as a prothrombin "control" in the routine laboratory procedure.

Since uropepsinogen is stable for days when kept at a suitable temperature in a refrigerator, in an emergency during weekends, a preoperative urine specimen could be obtained and stored until the laboratory staff resumes activities. For surgical follow-up studies, this affords a feature not present in many laboratory tests.

TABLE 3.—*Hematological Value of Uropepsinogen Determination*

Disease	No. of Cases	Uropepsinogen (Range), Mcg./Hr.	Uropepsinogen (Av.), Mcg./Hr.
Proved pernicious anemia	2	0.7—2.2	1.4
Suspected pernicious anemia (macrocytic anemia with histamine achlorhydria)	4	28.0—117.5	61.6

Results of Study

The results presented were obtained from a series of 57 cases. Since the compilation of these data, additional cases have been tested, and a cursory examination of the results reveals confirmatory evidence for the facts herein presented.

Table 1 depicts the difference between the normal value of uropepsinogen and those encountered in subjects with duodenal ulcers. Though the normal range overlaps those values found in the presence of the cases of duodenal ulcers, it should be pointed out that 92% of the patients with duodenal ulcers had higher values than the highest normal. Of the overlap group, 79% were greater than three times the mean normal. A thorough appraisal of this lower bracket revealed that each patient was on a strict ulcer therapy regimen at the time of the test, and none of these had an actual ulcer niche demonstrated roentgenographically. This influence of activity on the level of uropepsinogen has been noted by others.[14]

Table 2 [15] illustrates the value of uropepsinogen determinations in assessing the results of surgery. It might appear that vagotomy is a worthless procedure because it did not reduce the uropepsinogen content of the urine. This is not necessarily so; this finding merely indicates that at least the hormonal relationship still exists despite surgery. In the second case (table 2), despite the initial low level the uropepsinogen is reduced by approximately 65% postoperatively. Our findings agree with those of the Boston group where 26 such patients were studied.[5a]

As can be seen in this illustrative case of gastric ulcer, the level of uropepsinogen, falling within the normal range, is not diagnostic. This was true in three other cases, in which the range was 81.9 to 84.5, with a mean of 83.2 mcg. per hour. Uropepsinogen levels in cases of gastric malignancy, on the other hand, have been found by Gray[5a] to be considerably lower than those in patients with benign gastric ulcers. This was true in 61% of 53 patients with carcinoma, the level being zero in four cases of linitis plastica. In only three cases of malignancy in our series was the range 37.5 to 150.0 mcg. per hour. In these three examples, it can be seen that the uropepsinogen would have been of no diagnostic significance. It should be stated, however, that Gray's statistics correlate well with the well-documented higher incidence of carcinoma in hypofunctioning stomachs.

Table 4.—*Uropepsinogen Excretion Values in Various Disorders*

Case No	Suspected Diagnosis	X-Ray and Laboratory	Uropepsinogen, Mcg./Hr.	Final Diagnosis
1	Upper G.I. hemorrhage, probably marginal ulcer, dumping syndrome	G.I series negative; submucosal rectal carcinoma (by biopsy)	41.4	Submucosal rectal carcinoma
2	Surgical abdomen, etiology probable perforated duodenal ulcer	Serum amylase 448 units	133.9	Pancreatitis
3	Pituitary adenoma, previously diagnosed, now in remission	Eroded sella; 17-ketosteroids, B.P., and blood sugar normal	158.4	Same as suspected*
4	*Pituitary myxedema*	I [131] uptake 2.7; 17-ketosteroids (low), Kepler-power positive	7.8	Same as suspected
5	Laennec's cirrhosis, upper G.I. hemorrhage from probable peptic ulcer or esophageal varicosity	Prothrombin 29%, BSP (elevated), cephalin flocculation 4, bilirubin (elevated), albumin 1.7, globulin 7.0; G.I. series negative	73.0	Hypoprothrombinemia bleeding due to Laennec's cirrhosis
6	Uncontrolled diabetic, vomiting, etiology?	Guaiac negative stools, G.I. series showed duodenal irritability, no ulcer	59.2	Duodenitis
7	Alcoholic, upper G.I hemorrhage	Died before studies in x-ray (no autopsy)	79.0	Probable Laennec's cirrhosis with bleeding esophageal varicosity
8	Systemic lupus (not on steroid therapy)	Positive L.E. test	130.0	Same as suspected

* A patient with full-blown adrenocortical hyperfunction (Cushing's disease) tested by two of us[17] had a uropepsinogen level of 961.2 mcg. per hour.

Table 3 discloses the level of uropepsinogen in patients with proved pernicious anemia as compared with several suspected of having this condition. If a patient has achlorhydria refractory to histamine stimulation, has macrocytic anemia, and has been given vitamin B_{12}, so that studies of his bone marrow are not diagnostic, this test affords the fullest measure of assurance thus far devised in a simple test to rule out a diagnosis of pernicious anemia. If a patient has a normal uropepsinogen level, it can be unequivocably stated that he does not have pernicious anemia. Studies with vitamin B_{12} labeled with radioactive cobalt are more refined, but these require technical facilities not generally available. The importance of adequate renal function and the primacy of the target organ, the gastric mucosal gland, is apparent here in these cases of hypopepsinuria.

Table 4 illustrates the effect on the rate of excretion of pepsinogen in the urine in a variety of conditions. Some are of a controversial nature, and the differential value of the uropepsinogen determination becomes apparent. Case 7 of table 4 is noteworthy in that the patient died over a weekend, and rather suddenly, from exsanguination and shock. Yet, despite the lack of additional evidence, the urine specimen obtained prior to death afforded some measure of support to the presumptive diagnosis. The value of this simple test for uropepsinogen in evaluating a patient with an endocrine disturbance and one with massive upper gastrointestinal hemorrhage is indicated by the following case reports.

Report of Cases

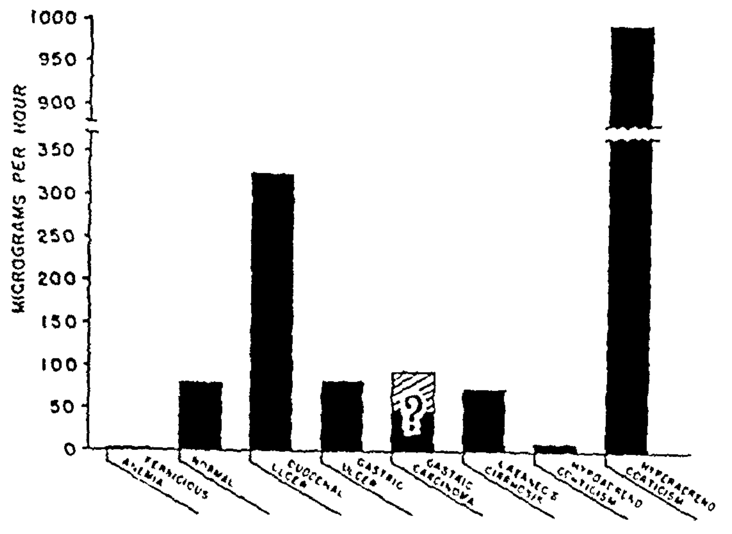
Case 1.—A 21-year-old woman noted increasing gain in weight, menstrual irregularity, and hirsutism. She was found to have borderline hypertension. Findings of a 17-ketosteroid excretion of 60 mg. per 24 hours prompted her referral to the endocrine clinic of the Pennsylvania Hospital. The endocrinologist, upon clinical evaluation, did not believe the patient had hyperadrenalcorticolism. A normal uropepsinogen value was confirmed by a normal 17-ketosteroid excretion determined in our laboratory. This patient with idiopathic hirsutism and exogenous obesity was spared expensive tests to rule out adrenocortical hyperfunction (Cushing's disease).

Case 2.—A Negro male, aged 68 years, with a 38-year history of excessive consumption of alcohol, was brought into the receiving ward in a state of shock. Hematemesis was observed, and rectal examination revealed a tarry stool. While the patient was assumed to be bleeding from esophageal varices, a balloon tamponade did not seal off the bleeding point. After 2,500 cc. of blood was given by transfusion, it became apparent it would be impossible to replace the blood fast enough; hence, an emergency gastrectomy was performed. Unfortunately, approximately six hours postoperatively the patient dislodged the endotracheal airway, vomited, aspirated a large amount of blood, and died. A preoperative uropepsinogen test revealed a level of 327.3 mcg. per hour. This is incompatible with Laennec's cirrhosis. At autopsy, gross and histological studies showed acute and chronic superficial hemorrhagic gastritis, not Laennec's cirrhosis.

It is apparent that, had routine measures to stop the flow of blood with a Sengstaken tube been continued, the patient would have died because of loss of blood. A simple urine test obtained when a barium swallow is not feasible might give the surgical member of a hemorrhage team the go-ahead signal, and the massive hemorrhage could thereby be controlled.

Comment

The figure is a graphic demonstration of the comparative levels of excretion of uropepsinogen in well and in diseased persons. The mean value for cases of duodenal ulcers is four times normal. The diagnostic value of this determination in excluding pernicious anemia is obvious when it is noted that the lowest normal value is approximately 14 times that of the highest value for cases of pernicious anemia (mean for pernicious anemia equals 1/55 of mean value for normal). The test is of no diagnostic value in a benign gastric ulcer, and its usefulness in differentiating the malignant lesion of the stomach is not determined. In the bleeding patient, its value is evident. It is probably too early to comment on the significance of the relationship of uropepsinogen to the adrenocortical-gastric axis. Suffice it to say, stress and psyche are well-known bedfellows, and both have been justly incriminated in the pathogenesis of disease. It may be reiterated, however, that, if the index of suspicion is high regarding adrenocortical hypofunction (Addison's disease) or adrenocortical hyperfunction (Cushing's disease), this test may be of special value.



Comparison of uropepsinogen levels (mean values) in well and diseased persons.

The department of rheumatology has recently undertaken a study[16] to test the reliability of this determination in "predicting" gastroduodenal complications of steroid therapy. Impetus to this investigation was recently afforded by a female patient with rheumatoid arthritis, who, without any previous gastrointestinal symptoms, suddenly suffered a perforation of a peptic ulcer.

Conclusions

If the simple technique of West, using Goodman's substrate and a curve standardized within the individual laboratory, is put to the test as the more controversial Anson and Mirsky method has been, the uropepsinogen determination may well find a place of real practical value among the tests that are simple to perform and that afford valuable clinical information.

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Dr. George R. Fisher, Chief of Endocrine Clinic, gave permission for use of case 1.

Dr. Edward H. McGehee, Hematologist, Pennsylvania Hospital, gave permission for use of the cases shown in table 3

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Postmastectomy Lymphedema.—The major factors in the production of lymphedema in the post-radical mastectomy arm are failure of muscular pump and anatomic disruption of lymph drainage channels. The failure of the muscular pump action of the extremity takes place in three stages. First the arm is necessarily immobilized in the immediate post-operative period. During this stage normal muscular action of the arm, particularly the shoulder girdle musculature, is prohibited. The second stage, disuse atrophy, occurs if immobilization is continued beyond a few days. In the final stage the patient may develop a frozen or partially limited shoulder, further inhibiting the use of the extremity and contributing further to the trend of disuse and hence failure of the muscular pump. Actual interruption of lymph drainage channels through the axilla is probably the major cause of the lymphedema; however, cases can be cited in which the lymph vessels and nodes were relatively spared and yet lymphedema developed. Apparently both disuse and channel interruption factors are operative in most cases. Physical treatment, prophylactic or definitive, is aimed at minimizing the effect of the two etiologic factors. Active motion of the shoulder should be initiated as soon as feasible post-operatively, certainly by the time the sutures are removed; partial range can often be prescribed safely a few days after operation, though full range exercises may have to be delayed. The patient should be instructed during the further recovery period to exercise the arm with increasing frequency and increasing resistance, even with the use of some household articles (such as a flatiron) for weights. It has been shown that muscular activity is an efficient method of moving lymph from an extremity.—C. Long II, M.D., *Physical Factors in Post-Mastectomy Lymphedema*, *Henry Ford Hospital Medical Bulletin*, June, 1956.

KINKING OF AORTIC ARCH (PSEUDOCOARCTATION, SUBCLINICAL COARCTATION)

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• *Roentgenographic evidence resembling a mediastinal tumor or coarctation of the aorta might, after careful study, prove to be a kinking of the aortic arch. Ten cases of this particular aortic deformity have been observed at the Mayo Clinic, four diagnosed in retrospect. Nine of the 10 patients had systolic murmurs at the base of the heart, probably the result of turbulence of blood in the region of the aortic kink. Oblique and lateral roentgenograms will usually allow the diagnosis of kinking, and confirmation can be had through angiocardiography.*

Kinking of the aortic arch is an anomaly that usually is recognized first by the appearance of the upper mediastinal shadow on the posteroanterior thoracic roentgenogram. The roentgenographic appearance frequently simulates that of a tumor adjacent to the aortic arch. Sometimes it brings to mind the deformity of the aorta that may be seen in coarctation. Furthermore, in roentgenograms taken in the lateral and left anterior oblique positions, a kink or buckle is seen in the aortic shadow, with its angular convexity at about the level of insertion of the ligamentum arteriosum.

This appearance of the aortic arch has resulted in the application of unsatisfactory and confusing names to this entity. For instance, it has been called "atypical coarctation,"[1] "subclinical coarctation,"[2] and "pseudocoarctation."[3] We prefer to adhere to noncommittal and, we believe, more accurate and less confusing designations, such as "buckling" or "kinking"[4] of the aorta. The first two of the following brief case reports present some of the features of this condition. These are taken from a group of six such cases encountered at the Mayo Clinic in which the diagnosis was made primarily.

Report of Cases

Case 1.—A 40-year-old woman first visited the Mayo Clinic in 1936 because of pain in her left sacroiliac region a few months after a fall. Her health had otherwise been good, although a cardiac murmur had been heard when she was 12 years of age. Results of examination in 1936 were essentially negative except for a basal systolic murmur of moderate intensity transmitted faintly to the vessels in the neck. The blood pressure was 150/86 mm. Hg. A roentgenogram of the thorax showed some torsion of the aorta. The patient visited the clinic on many occasions during the next 19 years, the last time being in 1955. In 1939, a stone was removed from the left ureter and hypoplasia of the right kidney was noted. Her visits often concerned episodes of thoracic pain that was thought to be consistent with angina pectoris, although the story was atypical. Her blood pressure gradually increased to 200/100 mm. Hg. Review of her electrocardiograms, including tracings recorded in 1955, revealed them to be normal aside from slight evidence of left ventricular hypertrophy. Over a period of 12 years, only minor changes occurred in the roentgenographic appearance of the cardiomediastinal configuration.

A number of roentgenologic diagnostic possibilities were entertained during observation of the patient in the above case, including aneurysm and mediastinal tumor. We now consider that the appearance of the upper mediastinum unquestionably is the result of a developmental kink or buckle of the aorta in the region of the ligamentum arteriosum (fig. 1). It is also extremely likely that this patient's murmur, discovered when she was 12 years of age, is a result of turbulence of the blood stream in the region of the aortic kink.

Case 2.—A 37-year-old woman registered at the clinic in 1954 with the main complaint of pain on swallowing. Six months previously, a thoracic roentgenogram had been taken and she had been told that she had an "enlarged blood vessel." Examination disclosed a grade 1 systolic murmur in the left infraclavicular zone transmitted to the left subclavian and carotid regions and faintly to the left upper interscapular region. Blood pressure in the arms and legs was normal. In a posteroanterior roentgenogram of the thorax, a small mass appeared to be projecting to the left at the level of the aortic arch (fig. 2*a*). This mass could not be disassociated fluoroscopically from the aortic arch. It showed evidence of pulsation, but it was impossible to tell whether the pulsation was transmitted or expansile. Therefore, angiocardiography was performed, which demonstrated that a peculiar buckle of the aortic arch was responsible for what appeared to be a mass (fig. 2*b* and *c*).

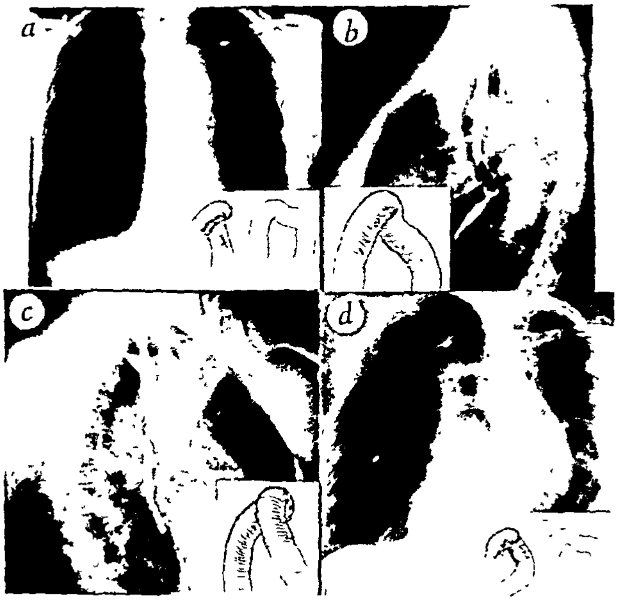

Fig. 1.—Roentgenograms of patient in case 1. Posteroanterior view, *a*, shows what appears to be a mass above aortic knob. Diagram indicates that the "mass" actually is the aortic knob, whereas what appears to be aortic knob is the segment of aorta beyond kink. Pronounced density at this point results from segment of arch beyond kink being seen "end on." Lateral, right anterior oblique, and left anterior views of aorta are shown in *b*, *c*, and *d*. The diagrams are self-explanatory. Note that aortic impression on barium-filled esophagus is made by segment of aorta beyond kink.

In another of the six cases there appeared to be some elongation and torsion of the aorta below the level of the kink, accentuating the abnormal appear-

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Read before the Section on Radiology at the 105th Annual Meeting of the American Medical Association, Chicago, June 13, 1956.

ance. With this in mind, we reviewed roentgenograms taken at the clinic during the last several years for which the designations "torsion of the aorta," "aneurysm of the thoracic aorta," and "left mediastinal mass" have been used. We suspected that we might find other instances of kinking of the aorta in which torsion had so distorted the appearance of the roentgenogram that it might simulate either a mass or an aneurysm. Also, we were interested to know what occurs in the region of the ligamentum when the thoracic aorta undergoes pronounced elongation.

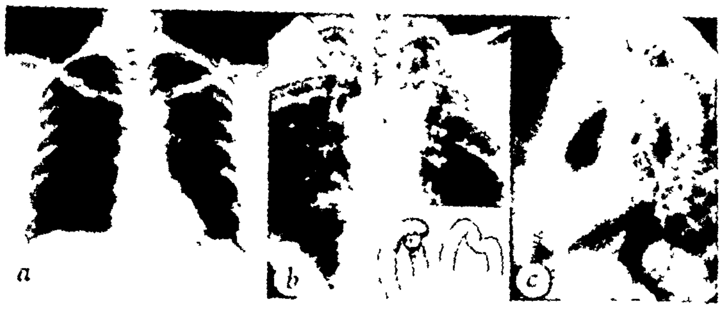

Fig. 2.—Roentgenograms of patient in case 2. Posteroanterior roentgenogram, *a*, shows double shadow at level of aortic knob. This could be interpreted reasonably as a mass adjacent to aortic knob or as aneurysmal dilatation of left subclavian artery. Angiocardiogram, *b*, in anteroposterior projection shows that the "mass" actually is aortic knob. Lateral angiocardiogram, *c*, indicating nature of aortic deformity. Arrows indicate highest level of aortic arch.

In the usual case of elongation of the aorta, the vessel takes a wide, smooth sweep over the left main bronchus and down the left paravertebral region, with enlargement of the "aortic window" (fig. 3). As the sweep of this arc increases in old age, we would surmise that either the intimate relations of the arch and left pulmonary artery are little disturbed or the tissues of the ligamentum stretch and degenerate without exerting a limiting effect on the unfolding process. If in certain cases the ligamentum did not stretch or degenerate, one might suspect that an elongated or tortuous aorta would be buckled at the site of insertion of the ligamentum. It is likely that the kink in a tortuous aorta described by Rösler and White [5] was of this nature. As the result of examination of many hundreds of roentgenograms, we found four instances of kinking of a tortuous aorta in the region of the ligamentum. One such case is presented.

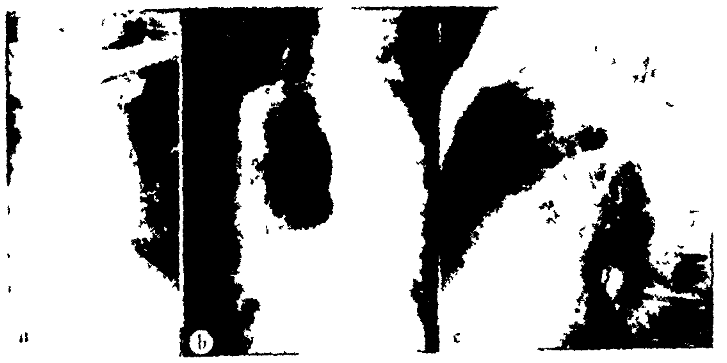

Fig. 3.—Roentgenograms showing, *a*, posteroanterior; *b*, left anterior oblique; and, *c*, lateral views of thorax demonstrating usual, smoothly rounded contour of a tortuous aorta.

Case 3.—A 52-year-old man came to the clinic because of hypertension. The blood pressure was 270/160 mm. Hg. Murmurs were not audible. Pulsations in the femoral artery were strong and not suggestive of coarctation. A roentgenogram of the thorax was suggestive of a mediastinal mass, possibly an aneurysm or a tumor (fig. 4*a*). Fluoroscopy and oblique and lateral roentgenograms showed a kink in the aorta in the vicinity of the ligamentum arteriosum (fig. 4*b* and *c*). The aorta was tortuous and elongated, with some dilatation immediately beyond the kink.

Clinical and Roentgenographic Observations

There is little in the literature on kinking of the aortic arch. Fewer than 30 cases have been reported or referred to.[6] It is likely that at least one of these cases has been reported twice. The best authenticated cases are one in which surgical exploration revealed the kink in the aorta to be at the site of insertion of a short patent ductus arteriosus [2] and one in which a retrograde aortogram revealed the kink to be at the site of a conically obliterated ductus arteriosus.[4a] The remarkable similarity of most of the published cases to each other would suggest that it is reasonable to assume that they are identical in cause to the two cases just mentioned. Roentgenologically, aortic kinking is of interest in that it so commonly simulates a mediastinal tumor. In the reported cases, as well as in some of our own, the practical significance of angiocardiography or retrograde aortography has been demonstrated, thereby obviating surgical exploration.

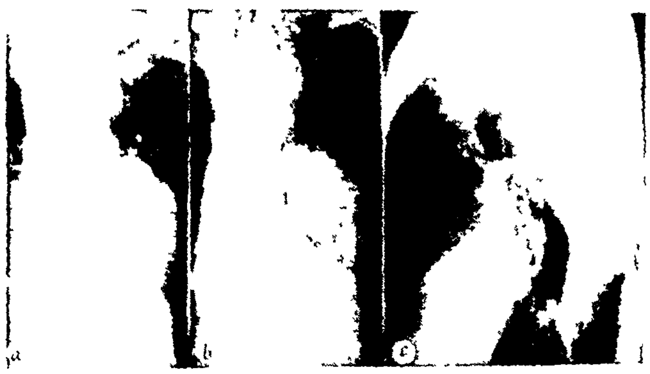

Fig. 4.—Roentgenograms of patient (case 3) with severe hypertension In posteroanterior roentgenogram, *a*, there appears to be a large mass at the left hilus. Heavier penetration, *b*, shows the "mass" extending down behind the heart. Lateral view, *c*, shows aorta kinked at level of left main bronchus (ligamentum); the "mass" is due to pronounced torsion and moderate dilatation.

The deformity of the aorta frequently seen in coarctation [7] is closely simulated in some of these cases, especially on posteroanterior roentgenograms This has given rise to the afore-mentioned designations of "pseudocoarctation" and "subclinical coarctation," terms that are not satisfactory. In their favor can be cited examples of patients with unquestionable coarctation who have lived to middle or old age without much disability and with relatively good pulses in the legs. However, to use the term "subclinical coarctation" for cases of kinked aorta in which other clinical or roentgenologic features of coarctation are absent is to make the untenable implication that the kinked aorta is a type of coarctation without coarctation. The fact that the kinking of the aorta occurs where the ligamentum arteriosum attaches to the aorta does not allow one to assume that such kinking is pathogenetically related to true coarctation. It is more likely that the aorta is kinked at that particular site because it is the logical location where traction would occur on the aorta. The predisposing cause for the kink is the traction of the ductus or ligamentum; the exciting cause is unknown but probably is related to an unusually short ligamentum or ductus or an unusually long aortic arch. Thus, we believe that "kinking" or "buckling" of the aorta is a preferable term and that the condition probably has nothing to do with true coarctation. Instances of "pseudocoarctation" could just as well be called "pseudotumor" because the posteroanterior roentgenograms in so many of them suggest the presence of a tumor. Furthermore, such lesions are never associated with notching of the ribs.

The usual presence of systolic murmurs in these patients if of interest. Nine of the 10 patients had systolic murmurs at the base of the heart, probably the result of turbulence of blood in the region of the aortic kink. In 2 of our 10 patients, murmurs had been detected in childhood and the patients had been told they had "leakage of the heart." In one of the patients referred to by Di Guglielmo and Guttadauro,[4a] the murmur had resulted in an inaccurate diagnosis of congenital heart disease.

Differential Diagnosis

The appearance of a mediastinal mass on the roentgenograms in their first case of kinked aorta led Souders and associates [2] to make a diagnosis of Hodgkin's disease. In three of the cases subsequently described in the literature, the suspicion of a mass was aroused by the appearance of the posteroanterior roentgenogram. Angiocardiography was performed in all these patients and revealed the true nature of the condition. As so commonly occurs, evaluation of a mediastinal mass is usually no clearer after fluoroscopy than it was before. In a recent study, Tucker and Bruwer [8] found that the interpretation of the roentgenograms was more often correct in the evaluation of a smooth-contoured left hilar mass than was the fluoroscopic interpretation. Furthermore, angiocardiography was vastly superior as a method of differentiating a mediastinal mass from a vascular shadow. In kinked aorta, a good oblique (usually a left anterior oblique) roentgenogram or a lateral roentgenogram usually will reveal the true state of affairs. If any further doubt remains, angiocardiography should be done.

Roentgenograms in cases of kinked aorta frequently give an appearance in which the aortic deformity simulates that seen in many cases of true coarctation. This similarity becomes more pronounced in those cases of true coarctation of the aorta in which roentgenologic evidence of notching of ribs is absent. Fluoroscopy may carry the similarity further, in that some aortic dilatation may be present beyond the anomaly in both conditions, and this can be well demonstrated by the impression of the dilated segment on the barium-filled esophagus. The differentiation from coarctation of the aorta depends on such findings as palpable collateral vessels, diminished pulses in the abdominal aorta and legs, hypertension in the upper extremities and disproportionately low blood pressure in the legs, and evidence of left ventricular enlargement.

Aneurysms may have to be differentiated, which requires investigations such as serologic tests for syphilis, inquiries into previous thoracic injuries, evaluation of oblique roentgenograms, and angiocardiography. Congenital aneurysms in the segment of the aorta between the origin of the left subclavian artery and the ductus arteriosus or ligamentum arteriosum usually show characteristic roentgenographic features.[9]

The murmurs that usually occur in patients with kinking of the aorta may lead to an unwarranted diagnosis of either congenital or acquired heart disease. Heart disease has been present in several cases,[10] but in most instances the murmurs are attributed best to turbulence of the blood stream in the kinked segment of the aorta.

Summary

Ten cases of kinked aortic arch have been encountered at the Mayo Clinic. The points of particular interest in this condition are that (1) it may resemble a mediastinal tumor on the posteroanterior roentgenogram; (2) it may bear roentgenographic resemblance to the aortic deformity that may occur in coarctation; and (3) the patients frequently have systolic murmurs that may give rise to an erroneous diagnosis of organic heart disease.

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10. Footnotes 3 and 4*a*

Intestinal Obstruction in Infants.—The most common cause of intestinal obstruction in the newborn is atresia. In a collective review of the subject in 1951, Evans estimated that each year 3,000 babies in the United States and 50,000 babies in the world are affected with this condition. The most commonly accepted etiologic theory is that during the fifth to twelfth week of intrauterine life the intestinal tract goes through a solid stage for a short period, that vacuoles then appear which coalesce and reestablish the lumen, and that an arrest in this vacuolization causes the atresia. Until recently, obstruction in the newborn was almost always fatal. Up until 1950 there were only 125 successfully treated cases recorded in the literature. Recovery is not a rarity today, but the mortality from intestinal obstruction remains high. Prematurity and associated anomalies are certainly the greatest cause of the high mortality, and not much can be done about those factors; but delay in diagnosis and treatment, which is a considerable factor, is subject to correction. Physicians who attend infants must constantly keep obstruction in mind.—O. Tuschka, M.D., and D. Hyde, M.D., Intestinal Obstruction in the Newborn, *California Medicine*, April, 1956.

ADVENTURE IN PEDAGOGY

George E. Miller, M.D., Buffalo

• *Twelve medical faculty members, with the conviction that medical education can be improved, undertook an investigative analysis of fundamental educational principles. In 20 hours of relatively unstructured discussion, using a chairman trained in sociology and anthropology and the dynamics of learning, there resulted a broadened understanding of and change in attitude toward the teaching processes being practiced. A few of the conclusions arrived at revealed that teachers may be major obstacles to student learning; that people learn what they want to learn; and that learning is largely an emotional experience. The student must be helped in wanting to learn rather than just to know.*

The results of this preliminary study, while giving certain participants a new self-awareness along with a new sensitivity to student needs, have made teaching far more difficult than before but have provided a personal satisfaction not previously known.

The long history of medical education on this continent has been marked by many turnings, which might lead an uninitiated observer to describe the path from student and preceptor of 1750 to the student and preceptor of 1950 as the completion of a full circle. The more generous would look upon it as a spiral in which each step was supported by those that went before. Among those steps three would stand out boldly: the steady increase in required years of formal education; the geometric progression of data to which the student is exposed, data that have been compounded in complexity as the contributions of chemists, mathematicians, and physicists have been incorporated into medical lore; and the fractionation of man into his component parts, each of which has been claimed by a belligerent corps demanding a larger share of the student's time. All of these things, Jay Tepperman has said, give our students a strange resemblance to "Belgian geese being fattened for *pâté de foie gras.*" It is perhaps a resulting sense of discontent that today has led us to reverse the field busily, to resynthesize the whole man with the help of sociologists, anthropologists, and clinical psychologists who have invaded our halls (to our enormous benefit, I need not add), and to slash away at course content, hoping our excisions will not remove some vital rung of the ladder a student must climb. Even the traditional structure of curriculum has been shaken by the demonstration that Western Reserve students, too, can pass national boards.

Need for Improvement in Quality

At the heart of this varied violence lies a conviction that improvement in the quality of medical education can be achieved. Yet there seems a curious omission in our methods. As physicians we regularly employ consultants who illuminate a problem by the special body of information or the particular competence they enjoy. But in our struggles as educators we ignore with equal regularity the potential contribution of those who have devoted their professional lives to the study and development of educational principle and practice. In all of higher education, including medicine, a degree and a clean collar are looked upon as adequate preparation for the heavy responsibility of teaching. Faced with this responsibility, most of us play it by ear and very shortly develop firm and unshakable belief in the propriety of what we are doing. This state of affairs is encouraged by the fairly general, if tacit, agreement that, if a man is appointed to a teaching position on the basis of scientific productiveness or professional competence, his proficiency as an educator will take care of itself. Perhaps the time has come to face up to the fact that many of us do not know what we are doing as teachers, that those of us who do learned it accidentally and cannot readily communicate it to others.

Investigation of Teaching-Learning Process

Such a confession is about as easy to make as an admission that one has no sense of humor. But, after two and one-half years of preliminary discussion, 12 University of Buffalo School of Medicine faculty members reached a point of willingness to accept this as a preliminary hypothesis. And with relatively open minds we set out to learn whether anything might be done to modify our ignorance of fundamental educational principles, if such actually existed.

In the selection of a guide to lead us through this wilderness, we were unusually fortunate. Nathaniel Cantor is administratively designated as the chairman of the department of sociology and anthropology in the college of arts and science and the school of education, but his interest and study has been the dynamics of learning. His vivid personality and disregard of professional jargon immediately dissipated the kind of communication barrier that at least three other medical schools encountered when they sought similar guidance from professional educators. Our group spent 20 hours together in relatively unstructured discussion, using as a resource only Cantor's book "The Teaching-Learning Process."[1] The broadened understanding and change in attitude that grew out of the experience was most dramatically demonstrated in tape recordings of the sessions. Although part of the impact is lost in transcription, I would like to describe several things that came sharply into focus.

We recognized very early that people learn what they want to learn. Of the many illustrations that immediately spring to mind, I might cite the student who

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From the University of Buffalo School of Medicine.

Adapted from a paper read before the Subsection on Medical Education of the American Federation for Clinical Research, Atlantic City, N. J., April 29, 1956.

has difficulty recalling the sequence of the Krebs cycle but may have at his finger tips the batting average of every player in the major leagues and the telephone numbers of 12 attractive girls. Shall we call him stupid, perverse? Or shall we dismiss the whole matter by remarking that he must be poorly motivated, since anyone who wants to be a physician should also want this piece of information. Such a comment relieves the teacher of any further responsibility, but it helps the student very little. It also implies that the teacher can decide what the student should want to know, which is patently absurd. But it does not deny the instructor an opportunity to help the student to want it. Let the teacher who will, establish a relationship between learning the Krebs cycle and becoming a physician, and he will be unable to stop the student from learning it eagerly and enthusiastically. For motivation relates not only to the distant goal but to each of the stepping stones that lead there. The teacher who asks the student to accept the relationship on faith asks more than he himself would be willing to give.

A closely related principle reminds us that knowledge and learning are different. In any medical faculty there is always a large body of opinion that emphasizes the importance of facts and encourages the accumulation of factual data through the simple device of making them the subject matter of examinations. This is done with complete sincerity in the belief that education is an intellectual exercise. But with a little insight the least of us could amass in a single hour an overwhelming body of evidence that true learning is largely an emotional experience. Most of what we learn at medical meetings vanishes overnight. The things we retain are those items that somehow kindle a spark, arouse curiosity, or incite anger or disagreement or laughter. And for each of us these things are different, for learning is also very personal. To concentrate upon facts, arbitrarily selected, as cold and bloodless things is to deny their vitality. Facts are too important to pass as idle conversation. We should not possess them. They should possess us.

We also reached agreement that true learning implies change. And here dilemma is encountered, for the first law of thermodynamics, the law of inertia, applies with equal force to the area of learning. In the course of 10 weeks, participants in these seminars became painfully aware of this principle. As some understanding of the dynamics of learning was gained, it was clear to all that we spent a good deal of time defending our own position on education, resisting change by any method we could devise, including the classic techniques we had seen our students use: tardiness, failure to read material previously agreed upon, shifting the focus of discussion when it came close to tender spots, obscuring the issue by vagueness, and indulging in hairsplitting, self-deception, and hostility.

But, under the skillful guidance of a leader who made no moral judgments of these tactics, who accepted them as an inevitable part of the learning process, who did not deny them by authoritarian dictums, progress and change took place, in a direction and at a pace that was acceptable to the group. The unskilled leader, failing to recognize these things, might have demanded that the group move in his direction, at his pace, and would have succeeded in blocking true learning by providing an object upon which resistance to change could be attached. It is frightening to recall how common this practice is in orthodox teaching, where change is expected, but only in the direction that the teacher, the authority, decrees.

If the first three principles are sound, the fourth, that true learning requires freedom, follows naturally. Whenever freedom in education is discussed, however, there is immediately an outcry from those who equate freedom with anarchy. Lest we fail to understand how men who have lived in a democracy can complete such an equation, we might recall that our educational system has usually been authoritarian (even in the heyday of free electives) and that teachers, too, resist change. Freedom is used here in the Websterian sense as the state of not being subject to an arbitrary external power. But who would deny that medical faculties in general, and physicians in particular, are often arbitrary in their exercise of power? A curriculum that is content-and-examination-centered provides freedom for the student to grow in only one way. And those schools that have liberalized their curriculums provide only as much freedom for individual student development as faculty members will allow. The usual tendency of a faculty is to encourage growth in its own image. The student who does what he is told, gives back the "official pitch" when he is called upon, and performs his work without question is usually looked upon as a good student, while the one who analyzes and challenges faculty statements and accepts nothing without supporting evidence is tagged an annoying little beast who probably needs a psychiatrist. The encouragement of this kind of student independence may make life considerably more trying for the teacher. Traditional teaching is relatively easy, but helping a student to learn is an exhausting occupation.

Role of Teacher

Examined in these terms, a more precise definition of the present role of the teacher in the learning process forces the conclusion that teachers may be major obstacles to student learning. It took participants in this seminar 12 hours to admit this openly. It would be unrealistic for me to expect a reader to accept it in 12 minutes. But the painful self-examination led us inevitably to such a terminus. Why? Because teachers of medicine are very much like everyone else. They have developed not only an understanding of a large body of data and a variety of technical skills but also an image of themselves. And whatever threatens this image is suppressed. The teacher preaches, and the student responds. The right answer is the answer the teacher wants, and both teacher and student often fail to recognize that true learning begins with not knowing the answer.

Students detect this long before they get to medical school, but most medical school teaching does nothing to suggest the desirability of change. How can they believe we encourage independence, when in biochemistry they are taught to reply that diabetes is the result of an overproduction of glucose while in physiology it is due to underutilization, and when in pediatrics only digitoxin can be used to treat congestive heart failure and in medicine only whole leaf digitalis? If they ask why these things are so, they are told in essence, "Because I say so." Not this crudely, I grant. But if one listens to tones, to shadings, to the meanings that words conceal rather than the words themselves, it becomes evident how rarely a teacher allows the image of himself to be threatened. Instead we use students to support this image. We expect them to defer to us, to respect and admire us, to mimic us, and to do well when examined by others on the material we are presumed to have taught them. And instead of giving them the help and encouragement they need, we exploit them for our own needs again and again.

The professional responsibility of the teacher should be obvious. It is based upon a fundamental respect for the individual student, an awareness of the dynamics of learning that must allow each student the freedom to be different and that encourages challenge. It is concerned with helping the student to want to learn rather than to know. It involves an honest effort to understand the student rather than to judge him. This should be easier for the physician-teacher to understand than for almost any other. The physician's occupation is to provide a professional service to patients. He attempts to understand their problems and to be of use in their solution. He makes no moral judgment of the illness and suffers no offense or loss of prestige if the patient ignores his advice or fails to respond to his best therapeutic efforts. He is secure in his role. It is this kind of professional service that the teacher owes the student and, if he gives less, he is a fraud.

While this indictment is broad, it does not include all medical teachers. And, of those it does embrace, a significant number might say that they would like to teach in this understanding, challenging, encouraging way but are forced by departmental policy, curriculum arrangement, state and national board examinations, or some other restriction to conduct themselves in an orthodox, authoritarian fashion that they recognize as second rate. This brings me to the final point, the nature of compromise. There are realities that we all must face. There are limits beyond which we cannot go, limits of time and space, external and internal forces that must be respected. To recognize such limitations, however, is quite different from using them as an excuse for not doing something you really do not want to do anyway. As Cantor puts it, "Even in a strait jacket there is room for some movement." We do what we can when we can do it. But first we must understand ourselves.

Results of Investigation

One might properly ask what happened to the faculty members who went through this experience. I can answer that none of them has been dismissed for heretical teaching. We have no quantitative measure of their change nor any evaluation of its quality. But 9 of the 12 have a new awareness of themselves, a new sensitivity to their students' problems. They find teaching a much more difficult task than it was before, but it provides them with a satisfaction they had not previously known. And they recognize their limitations, their need for further growth and development as teachers.

Because of this outcome we have been encouraged to travel further down this avenue, which seems to lead toward an important juncture of the problem in medical education. With generous support from the Commonwealth Fund, a more elaborate program has been developed, which will allow members of our own faculty, with selected visiting faculty from other medical schools, to explore in greater depth such fundamental principles of education as these and to put them to the test of practice in a medical context. Under medical school direction, an annual series of seminars and workshops, beginning in September, 1956, will continue to use the wealth of skill and information in the school of education and college of arts and sciences that might contribute to a solution of the problems we face as medical educators.

In addition to the teaching-learning process, it has seemed worthwhile to investigate, in such seminars, the nature of the medical student, who he is, and where he comes from, what his background is in psychological and socioeconomic terms, how the selection process influences his development before he arrives in medical school and the kind of response he makes to a medical curriculum, what the effect of the medical school environment is upon his ability to learn and to grow, and what kind of person he becomes professionally and socially. Some attention will also be given to the evolution of higher education in general and medical education in particular, for it is difficult to comprehend where we are or where we are going without some knowledge of where we have been. The broad field of evaluation of the outcomes of learning in a medical setting will also be considered: Are our present methods truly evaluation or simply measurement of acquired information? What are the principles that underlie the selection of a specific technique? How may the variety of evaluation techniques be most effectively incorporated into the educational pattern of medicine? Finally, some attention will be devoted to the broad subject of communication, the methods and materials of instruction. But only finally, for methodology is simply handmaiden to principle; without principles methods become empty and isolated efforts.

Is it all worthwhile? My biased opinion is often balanced by those who call this talk of educational principles nonsense, who remind me that the work of the teacher is to cram into the student as many facts as possible in the time allotted. (They further point out that the time allotted their subject is not enough.) And they may be right. But while they man their bastions against attack, we, the enemy, will be having a rousing adventure in pedagogy.

3435 Main St. (14).

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ANTIGENIC POTENCY OF POLIOMYELITIS VACCINE

INFLUENCE ON DEGREE AND DURATION OF VACCINE EFFECT

Jonas E. Salk, M.D., Pittsburgh

• *Groups of children who had been given different doses of a poliomyelitis reference vaccine A in the spring of 1955 were all reinoculated in the spring of 1956 with the same dosage of vaccine J. Quantitative studies demonstrated both the persistence of the antibody over the course of a year and the increase in titer in response to the third dose given at this time. To secure an optimum response to the booster injections it was necessary to give an adequate dose in the primary antigenic stimulation. After the booster injections the antibody titers equaled or exceeded those found in a group of convalescents from recent type 1 paralytic poliomyelitis. The nonliving, nonmultiplying virus antigen reproduced the serologic effects of naturally acquired infection-immunity. Seven lots of commercially prepared vaccines administered to 186 subjects, compared with five lots of laboratory-prepared vaccine in 115 subjects, proved to be equally satisfactory as to potency and uniformity in raising the antibody titer. In 4,617 subjects who received three inoculations, only 224 had antibody at a level of 1:64 for all three types before inoculation, but 4,548 had antibody at this level for all three types after the third inoculation. Six lots of commercially prepared vaccine were used in a study of 214 subjects as to the advantages of a second inoculation, and the rise in titer produced by the second inoculation was clearly demonstrated for each lot, so that a low proportion of response to the first dose was converted to a high proportion of response by the second dose.*

As a result of recent studies on vaccination against poliomyelitis, much information on the immunology of this disease has accumulated. The purpose of this paper is to present a number of facts on the basis of which immunologic thinking has been clarified and a practicable method of immunization devised. Before presenting the immunologic problems, it might be well to review very briefly the effect of the experience of the past year upon the question of safety, this being the foremost of the two considerations of practicality, i. e., safety and effectiveness.

Vaccine Safety

It is self-evident that, for vaccination against poliomyelitis to be practicable, it must not be attended by any risk that would tend to discourage its use. In preliminary studies and in the field trial it was established that antibody production and immunity can be induced without risk of inducing paralysis; this has been reaffirmed in an accumulating experience in the United States and in other countries. It is now clear that this vaccination procedure does not necessarily possess an inherent risk, and this is true regardless of the nature of the strains of virus employed.[1]

The destruction of infectivity of poliomyelitis virus by formaldehyde is an orderly chemical process and, when properly carried out, with due attention to details and to the principles involved, results in a reliably predictable effect.[1] Although safety tests are performed on a relatively small fraction of each batch, they provide a substantial degree of confidence. In addition, the index of safety for each batch in a given series can be extended, far beyond the degree of assurance that the test of a single batch provides, by using the safety test as an indicator of consistency, or as a measure of reliability, of the manufacturing process. The concept of the "built-in safety factors" of the process, together with the required tests applied during processing and at the end, and, of equal importance, the reasonable interpretation of test results, have resulted in an order of safety that extends by a considerable margin the degree of confidence provided by the results of tests of each individual vaccine lot.

The several inferences[2] that the theoretical considerations were unsound, or were not applicable under conditions of large scale manufacture, seem not to have been supported by time. These inferences were drawn from the misinterpretation of failures of inactivation as having theoretical significance. When the occurrence of inactivation failures was interpreted as indicating need for attention to technical details and when corrections were introduced, consistency was achieved; the importance of consistency as an applicable requirement for safety then became generally accepted.[3]

Immunologic Objectives

Even though it will not be necessary for elimination of epidemics of poliomyelitis to await full vaccination of all susceptible persons, the nature of the infectious process, and of the immune mechanism, is such that it would be desirable for vaccination to be effective in each individual inoculated. It would be desirable, too, that there be a high degree of confidence that the protective effect, once induced, persists for long periods of time—preferably for the lifetime of the individual. Although it is too soon to be concerned, in a practical sense, about duration of immunity in terms of lifelong effects, since the full potential of the initial effects is still to be demonstrated, there is, nevertheless, sufficient basis for considering, from the theoretical viewpoint, whether immunity is likely to be of long or short duration. Data now available, when considered in the light of the immunologic principles and mechanisms involved, permit interpreta-

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From the Virus Research Laboratory, School of Medicine, University of Pittsburgh.

Read before the General Scientific Meetings at the 105th Annual Meeting of the American Medical Association, Chicago, June 11, 1956.

tions and predictions concerning durability of immunity and probable degree of effectiveness. Time will reveal the reasonableness of any predictions that may be inferred and the extent to which the data now available have been critically examined and soundly interpreted.

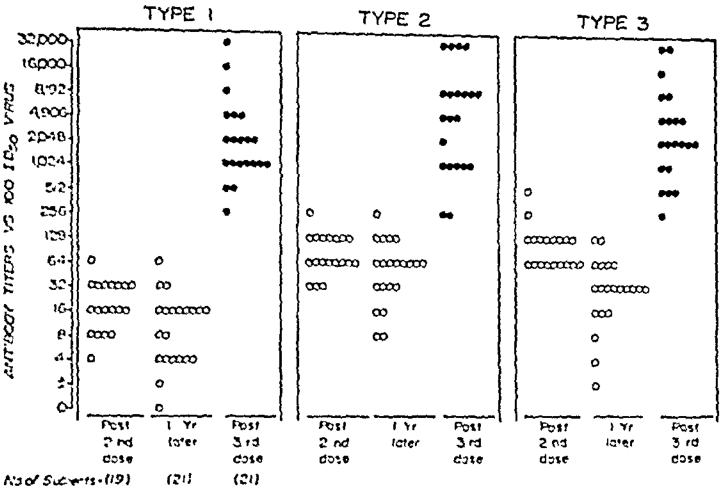

Fig. 1.—Persistence of primary response and degree of booster response. Two 1-ml. doses of reference vaccine A given two weeks apart and 1-ml. dose of vaccine J given one year later in children without antibody for any type before vaccination (± = trace of antibody at 1:4 dilution; 0 = antibody level lower than 1:4).

Mechanism of Immunity

Many studies have shown that immunity to paralysis exists when antibody is present in the serum.[4] More recently it has been revealed[5] that, if a state of immunologic hyperreactivity exists, immunity to paralysis can also exist, even in the absence of a demonstrable level of circulating antibody. This observation has now been confirmed by others[6] and reaffirmed in the further extensions of our studies.[7] Hyperreactivity must be of such degree that, after contact with virus, antibody formation will begin sufficiently rapidly to intercept virus before it can reach the central nervous system. Since the incubation period after natural exposure, and before invasion of the central nervous system, is 10 to 12 days,[8] and sometimes longer, it is understandable how a mechanism such as this does operate in the prevention of paralysis in poliomyelitis. As pointed out many years ago by Paul,[8] and referred to again by Bodian[9] and by Horstmann,[10] paralysis in poliomyelitis is a secondary consequence of a primary systemic infection. Thus, if immunologic hyperreactivity is induced by vaccination, then subsequent contact with the virus under natural circumstances should occur without risk of paralysis, since accelerated antibody formation should prevent invasion of the central nervous system, even though the pharyngeal or intestinal infection had not been prevented.

There is evidence from animal experiments that indicates that just demonstrable levels of serum antibody appear to be adequate for preventing invasion of the central nervous system. However, evidence from field tests of the prophylactic effect of gamma globulin[11] and of a single dose of vaccine[12] suggests that levels of antibody just below the range of detectability are also protective against paralysis. Further evidence, referred to above,[5] illustrates that, in cases where antibody is not detectable, paralysis may be prevented if re-formation of antibody is sufficiently accelerated to provide effective concentrations prior to the time when invasion of the central nervous system might occur. Depending upon the degree of immunity engendered, infection may be limited in such a way that paralysis does not ensue; however, if the intensity of the immunity induced is sufficient, virus multiplication at the portal of entry may be limited even to the extent that the establishment of infection is prevented.[13] Evidence in support of this has been reported by Howe[14] in studies with chimpanzees.

Immunologic Effects of Vaccination

Although there is wide variation in antibody response among individuals, it is evident from available data that vaccine potency does not influence the degree of variation in response among individuals, even though it does affect the level at which the variations occur. When vaccine dosage is varied within certain limits, the mean response induced varies with the size of the dose. Because of the wide range of variation of individual responses, discrimination between vaccines, with respect to relative potency, cannot be made by studies in single subjects; studies in groups of reasonable size will reveal the quantitative aspect of the dosage-response relationships.

In studies reported previously, it was shown that vaccine potency affects the degree of primary antibody response. However, it was not known to what extent the potency of vaccine used for primary stimulation affects the degree of secondary, or booster, response. Accordingly, groups of children who had been given different doses of reference vaccine A, in the spring of 1955, were all reinoculated in the spring of 1956, with the same dosage of vaccine J. The kind of results obtained are shown in figure 1, which illustrates the levels of antibody observed two weeks after the second dose of 1 ml. of reference vaccine A, the persistence over the course of a year, and the response to the third dose given at this time. The findings, following each of the different dosages of reference vaccine, are summarized in figure 2, which indicates the geometric

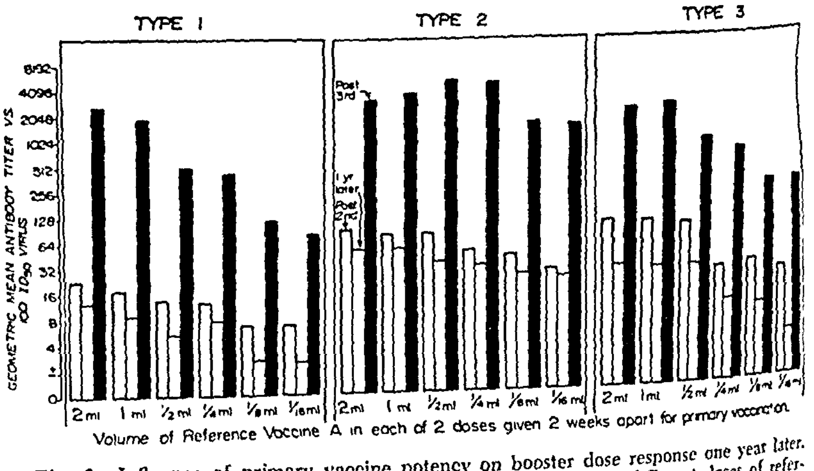

Fig. 2.—Influence of primary vaccine potency on booster dose response one year later. Groups of 20-30 subjects with no prevaccination antibody given different doses of reference vaccine A and 1 ml. of vaccine J given one year later.

mean levels observed at each of these intervals. It is apparent from the data for types 1 and 3 that the degree of response to the booster injection was affected by the dose of vaccine used for primary antigenic stimulation. This relationship is less evident for the type 2 component. Although the reason for this difference is not fully understood, it may, in part, be explained if the concentration of type 2 antigen in this vaccine is in sufficient excess so as to have shifted the range of the response to the plateau portion and away from the steep portion of the sigmoid curve that usually describes dosage-response effects of this kind. Attention has been called previously to the difference in antigenic behavior of the type 2 antigen insofar as it seems to exert a more potent effect than the types 1 and 3 antigens.

Antibody response after the third dose in each person is shown in figures 3 and 4. It is of interest that all in these groups developed a measurable level of antibody after three doses of vaccine, even though there was as much as a thirty-two-fold difference in potency of the material used for primary vaccination. The data in figure 3 show, also for comparison, the levels of antibody observed in a group of recent convalescents from type 1 paralytic poliomyelitis. The vaccine of higher potency induced levels of antibody equal to, or greater than, those observed after a naturally acquired paralyzing infection, whereas vaccine of lesser potency induced effects that were measurably less than those induced by infection. Thus, it is evident that it is possible to equal or to exceed the immunologic effects that follow infection, if attention is given to the quantitative factors that influence immunologic reactivity to a noninfectious vaccine. It would follow from this, therefore, that it is not necessary to use infective virus to simulate the effects of naturally acquired infection-immunity, since the immunologic effects can be reproduced by a nonliving, nonmultiplying virus antigen. This is not a new concept in immunology, but one that has not been as widely accepted as the evidence appears to warrant.

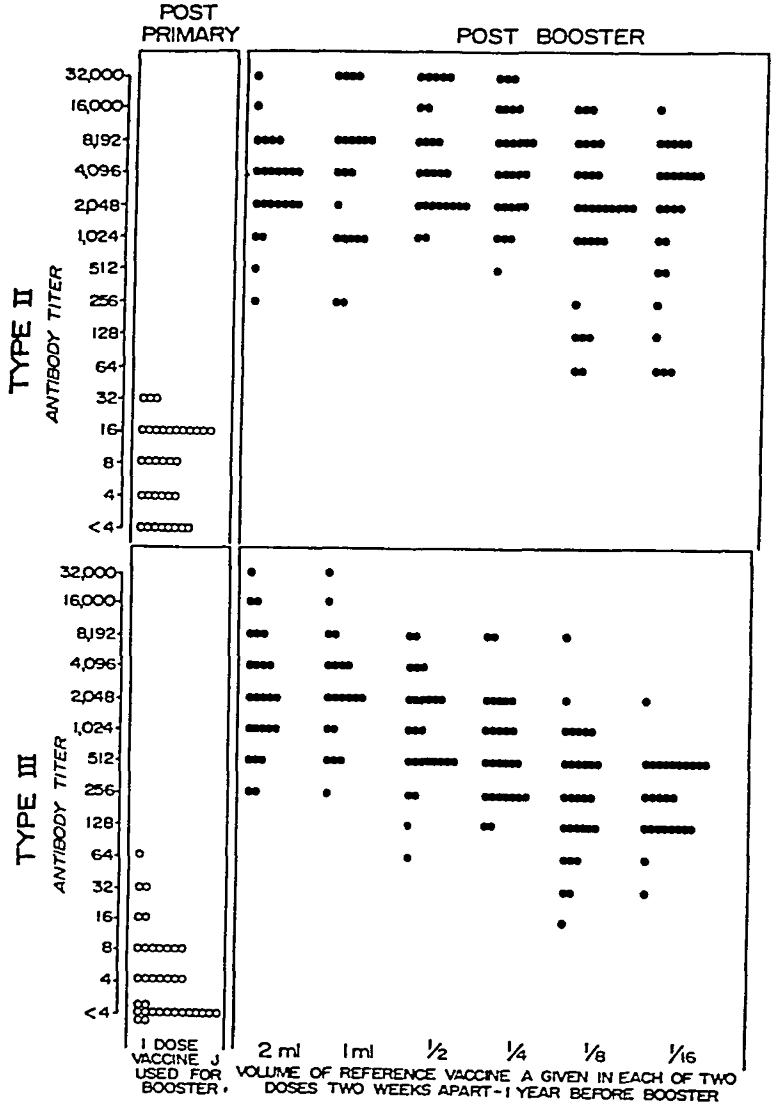

Fig. 4.—Antibody response (types 2 and 3) after booster dose in relation to potency of vaccine used for primary inoculation.

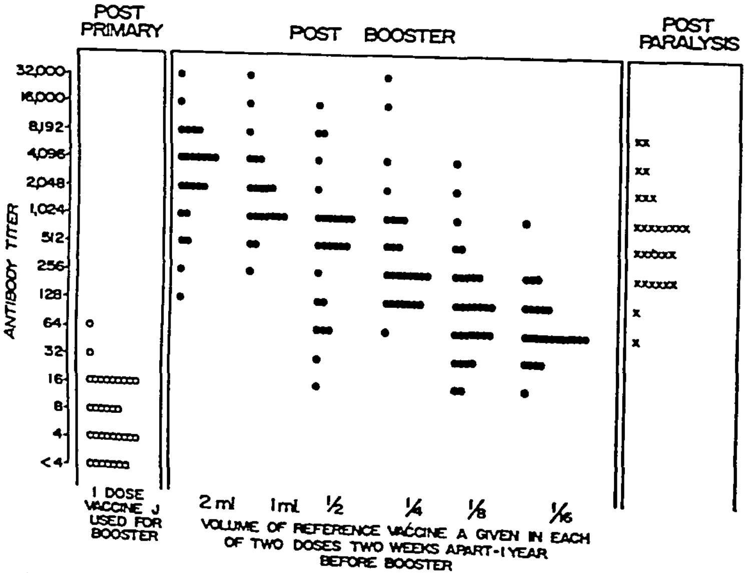

Fig. 3.—Type 1 antibody response after booster dose in relation to potency of vaccine used for primary inoculation and as compared with antibody titer following natural infection.

To illustrate the extent to which commercially produced vaccine can and has induced effects similar to those described for laboratory produced material, a comparison is shown in figure 5 to illustrate the levels of type 1 antibody that developed after the third dose in children with no prevaccination antibody for any type who had, one year earlier, received two doses, two weeks apart, of vaccine produced for general use. There were seven lots of commercial vaccine and five lots of vaccine produced in this laboratory. The vaccine used for the third dose was one of average potency from among the group for which the data on laboratory produced vaccine are shown; the response to a single dose of the vaccine J used for "booster" is also shown in figure 5, and was shown in figures 3 and 4. It will be necessary to study in more detail those individuals in whom there seemed to be less response than for the average, and to determine, if possible, the factors that might be responsible; there has not yet been time to repeat these tests.

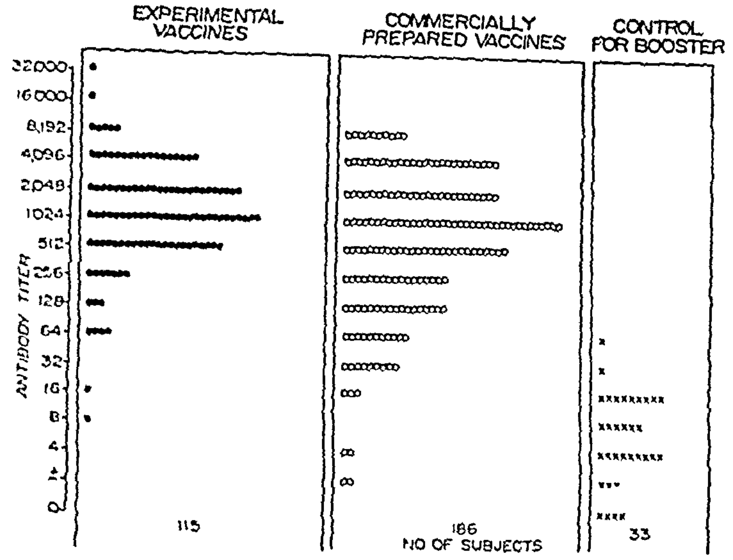

Fig. 5.—Comparison of experimental and commercially prepared vaccine. Type 1 antibody titers after booster dose with vaccine J in groups with no prevaccination antibody given two primary doses with vaccines indicated.

The point of particular significance is the fact, evident from an examination of data on the seven individual vaccine lots (fig. 6), that the variation in type 1 potency of five of the seven lots did not differ significantly from that of the experimentally produced vaccine. Thus, it would appear that the potency test, as employed for discriminating between lots of vaccine, could be expected to produce the degree of consistency here observed, when the criteria used to guide selections are those suggested by these data.

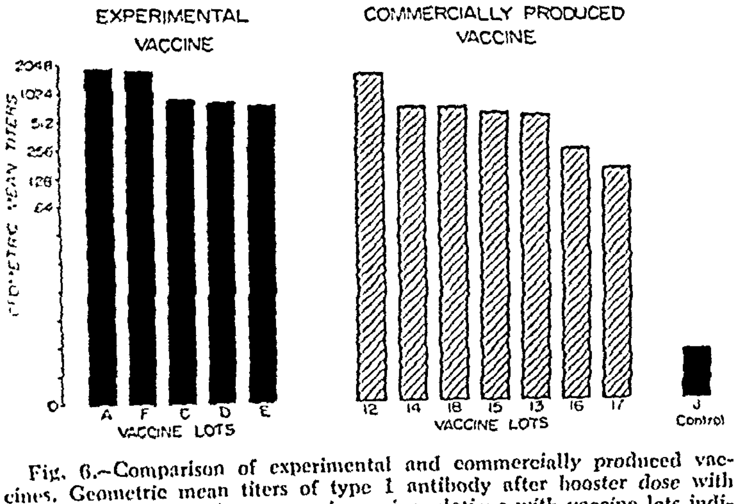

Fig. 6.—Comparison of experimental and commercially produced vaccines. Geometric mean titers of type 1 antibody after booster dose with vaccine J in groups given two primary inoculations with vaccine lots indicated.

As was to be expected, and as is clear from the foregoing data, individual variation in responsiveness to vaccination exists, just as does variation in immunologic response to infection; however, it is also clear that the significance of such variation, in terms of the prevention of disease, can be reduced by the administration of sufficiently potent vaccine and by adequately spaced multiple inoculations. Thus, there are some individuals who do not respond to the first dose of vaccine but who would have responded if potency had been greater. On the other hand, the use of multiple inoculations provides a more efficient way of insuring uniform response—a fact well known in immunology and demonstrated again in man and in experimental animals.

The objective to be achieved, either by increasing antigenic potency or by the use of multiple inoculations, is the conversion of all who have no antibody to any of the three types to a state in which they possess antibody to all three types. The degree of success that it has been possible to achieve in groups larger than those described in the data presented thus far can be illustrated by results of studies in groups consisting of more than 5,000 school children. A simplified procedure for determining antibody response was used, but one that puts vaccination to a particularly severe test. The procedure employed involved the determination of the presence or absence of antibody in a drop of blood from a finger-prick, tested in such a way that the positive or negative result indicated the presence or absence of antibody in a serum dilution of 1:64 as measured against approximately 100 T.C.I.D.$_{50}$ (tissue culture infectious doses) of virus of each type. Although a positive test for antibody indicated that it was present at a serum dilution of 1:64 or greater, a negative test did not necessarily mean that antibody for the particular type was not present.

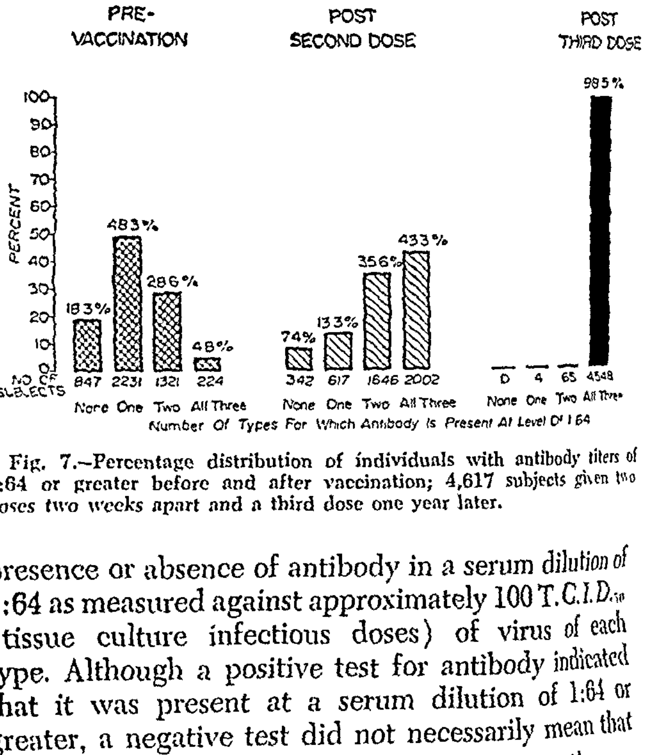

Fig. 7.—Percentage distribution of individuals with antibody titers of 1:64 or greater before and after vaccination; 4,617 subjects given two doses two weeks apart and a third dose one year later.

From figure 7 it is seen that, before vaccination, of the 4,617 subjects who had received three inoculations and for whom blood test information was available, only 224 had antibody at a level of 1:64 for all three types; 1,321 had antibody for two types, 2,231 had antibody for one type only; and 847 had no antibody for any type detectable at a level of 1:64. After two doses of vaccine, given two weeks apart, there was a shift in pattern, which is shown in the center set of columns and which indicates a reduction in proportion of those with no antibody, or antibody for but one type, and an increase in the proportion of those with antibody for two or three types, at a level of 1:64 or greater. After the third dose, given one year later, the shift was such that 4,548 out of the total of 4,617, or 98.5%, had antibody for all three types, at this level.

The effects described were induced with the use of two doses, 1 ml. intramuscularly for each dose given two weeks apart, of commercially prepared vaccine, followed one year later by 1 ml. intramuscularly of laboratory prepared vaccine of average potency as compared with commercially prepared material. The vaccines used are the same as those referred to in figures 5 and 6.

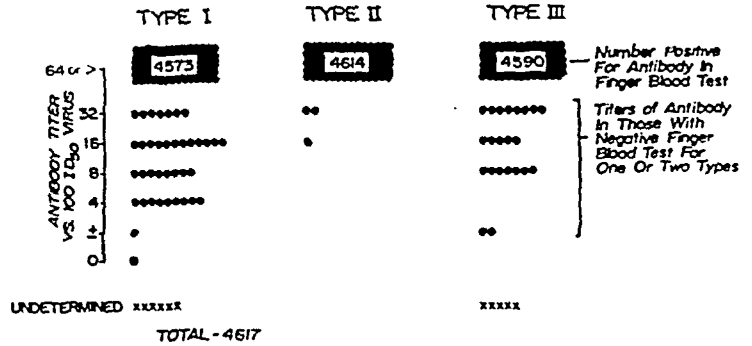

Fig. 8.—Antibody levels determined on samples of venous blood after three doses of vaccine in those who gave negative finger blood test for antibody at level of 1:64.

An effort was made to determine whether the 69 (fig. 7) in whom there was no detectable antibody for one or two types, at the 1:64 level, had antibody at lower levels of detectability. Accordingly, venous blood samples were obtained from all but 11 children: the results are summarized in figure 8. From these data it is clear that the separation of positives and negatives at a level of 1:64, using the finger blood test, greatly simplified the separation of those who needed more detailed study. Thus, a positive test for antibody at a level of 1:64 is indication of the presence of a substantial concentration of serum antibody; but, a negative test does not necessarily indicate that antibody is not present. In fact, in only one instance was antibody not detectable at a level of 1:4. Further investigation and studies are under way to determine the possible reasons for these results or for the low degree of immunologic reactivity, if these observations are confirmed, in all instances, upon retest.

The effect of the three doses in the 847 children (fig. 7) without antibody for any of the three types, at a level of 1:64, is shown in figure 9. It can be seen that there was a reduction to zero in the number with no antibody for any type, but 44 had no antibody, at a level of 1:64, for one or two types. The distribution of antibody titers in these individuals is as shown (fig. 9), and it is seen that antibody was detectable in all but one instance. Since all had responded with good levels to the type 2 component of the vaccine, these findings suggest that the poor responses were not due merely to a low capacity to respond but, also, to differences in relative potencies of the three types.

Effect of One and Two Doses of Vaccine

The advantage of two doses of vaccine, as compared with one dose, in terms of antibody response, is illustrated in figure 10. This shows the degree of response induced in groups of children who had no antibody for any type prior to vaccination and who were given two doses of vaccine four weeks apart. Six lots of commercially prepared vaccine were involved in this study. Titers of antibody were measured four weeks after the first dose and two weeks after the second dose.

In an effort to establish the significance of these measurements, an attempt was made to estimate the degree of correlation between protective effect and immunologic response to one dose of vaccine. Such information could be had from the 1955 epidemic in Massachusetts, caused by the type 1 virus. Studies were made, therefore, of the three lots of vaccine used in Massachusetts in the preceding spring. Children, with no preantibody to any type, were inoculated and antibody levels determined after one and two doses, given four weeks apart. These results are shown in figure 11, where it is seen that the low proportion of response to the first dose was converted to a high proportion by the second dose. It is reported that the protective effect of a single dose against paralytic poliomyelitis in the Massachusetts epidemic was 60 to 65%.[15] This degree of protection is greater than is the percentage response with antibody titers of 1:4 or greater, especially for lot 028849, which was used to a greater extent than the other two.

It should be kept in mind that a negative test for antibody at a 1:4 dilution of serum, according to the serologic method employed, indicates that antibody is not detectable in 0.06 ml. of serum when tested against 100 T. C. I. D.$_{50}$. This is a severe test and does not exclude the possibility that virus neutralizing effect would be demonstrable if a larger volume of serum were allowed to react with the same or a smaller amount of virus. Since it appears that protection may be associated with levels that are too low to be measurable by the test that is employed, it would seem conservative to infer that antibody levels of 1:4 or greater could be expected to be protective.

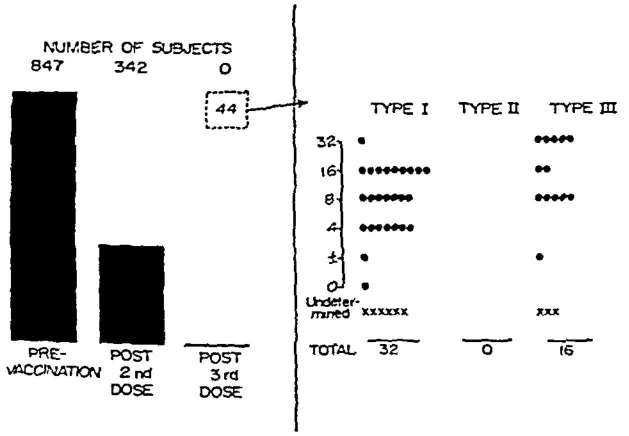

Fig. 9.—*Left*, effect of three doses of vaccine on 847 children with no antibody for all three types at level of 1:64. *Right*, antibody levels determined on samples of venous blood after three doses of vaccine in 44 subjects who have negative finger blood test for antibody at level of 1:64.

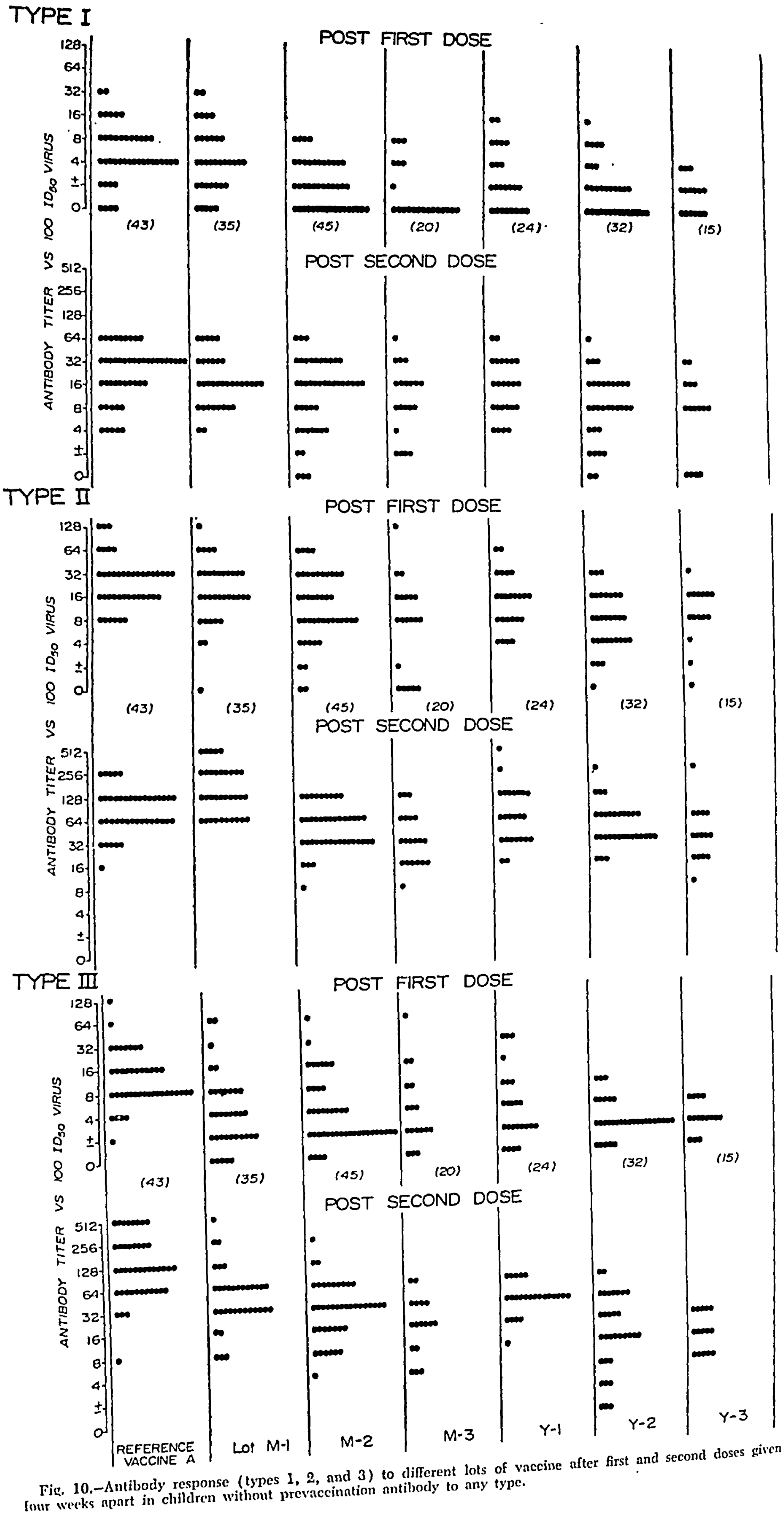

Fig. 10.—Antibody response (types 1, 2, and 3) to different lots of vaccine after first and second doses given four weeks apart in children without prevaccination antibody to any type.

Comment

The objective of these studies was to clarify our understanding sufficiently to permit the establishment of a set of conditions that would, under practical circumstances, produce an effect with a wide margin between the lowest individual response induced and the minimal response that might be required for immunity. In this way it was hoped to approach the irreducible minimum for the number of individuals who fail to respond with a significant degree of immunity.

From these studies it appears that the level of antibody induced, and its degree of persistence, at demonstrable levels, is a function primarily of mass of virus antigen injected, of the number of doses into which this is divided, and of the spacing between doses. The question then arises as to what constitutes adequate antigenic mass and adequate numbers of inoculations. It has been observed, even in individuals who have had minimal antigenic stimulation, and in some intances with no elicitation of antibody response, that there has been induced, nevertheless, a state of hyperreactivity demonstrable by reinoculation after the lapse of a sufficient interval of time. However, from the practical viewpoint of inducing immunity, it would not be reasonable to rely upon the development of immunologic hyperreactivity without the creation, at the same time, of a measurable antibody response. Since the hyperreactivity that develops also seems to persist, if an antibody response was once elicited, it would be more reasonable to aim at inducing the formation of a sufficient level of antibody to be certain that a hyperreactive state has also been created. That a substantial degree of hyperreactivity has been developed may be measured by comparing the degree of antibody response induced after the "booster" with the response to a similar dose of vaccine given to a group of immunologically inexperienced persons. Such effects are demonstrated in figures 3 and 4, which show the distribution of antibody titers before and after a single dose of vaccine J in a group of previously vaccinated persons and in a group not previously treated. The lowest response in the previously sensitized group is equal to or greater than the highest response in the group not previously sensitized.

In the course of these studies, it has been noted not only that that intensity of primary sensitization influences the degree of antibody response but that the booster dose is no more effective than a first injection if the vaccine used in the primary series possessed little or no antigenic activity. This observation was reported earlier and its importance has been mentioned previously. The pertinent findings, shown in figure 12, which illustrate merely a primary response to a so-called booster dose, given 10 months after the primary series, serve as the basis for the recommendation that children who participated in the field trial and who received vaccine that, according to present standards, may have been less than optimal in potency, should receive three doses, as if they had not been vaccinated previously, and that this be administered with intervals suggested by the findings in these investigations. This was discussed in detail in the May 26, 1956, issue of THE JOURNAL.[16]

The questions that confront the physician who administers poliomyelitis virus vaccine are: "How certain am I of the beneficial effects that it is intended to produce? How long will the effect last? Do I have to administer reinoculations and, if so, when? What is the probability that each of my patients individually will escape paralytic poliomyelitis?" These are also questions that are asked by an enlightened public. If the immunologic factors that are operative are understood, patients will more readily cooperate with physicians in the practice of the prevention of this disease, even though this will become more difficult as the fear that is now imposed by the occurrence of epidemics is eliminated.

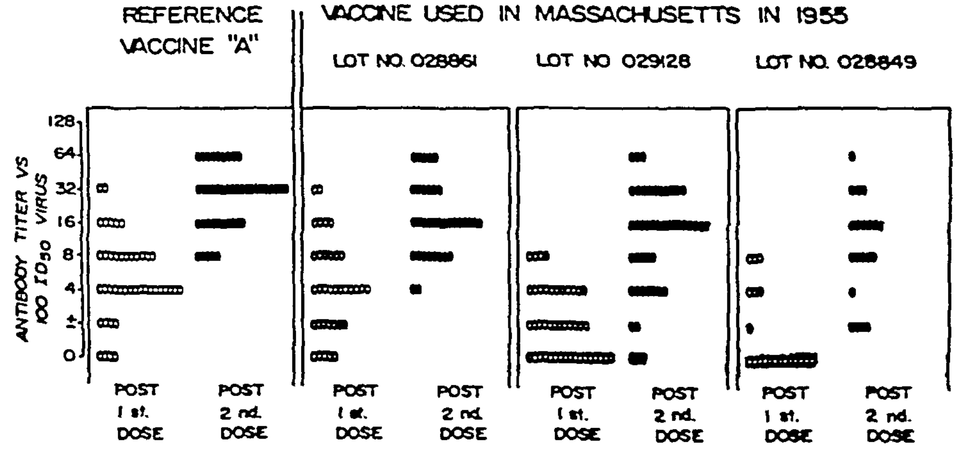

Fig. 11.—Type 1 antibody response after first and second doses of vaccine lots used in the spring of 1955 in Massachusetts.

The answers to the practical questions of consistency of degree of effectiveness and probable duration of immunity are best expressed in terms of the results of studies that were designed to reveal the factors, both quantitative and qualitative, that contribute to variation in individual and in group response. It is clear that the amount of virus antigen injected is the chief determinant of the intensity of the immune response; this is reflected either in level of antibody induced or in degree of immunologic hyperreactivity effected. It has been shown, also, that the amount of virus antigen required to induce a maximal immunologic effect is substantially less if multiple injections are administered and if adequate attention is given to the spacing between inoculations.

Although the efficiency of the effect of multiple injections is greater as the interval between inoculations is prolonged, at least to a certain point, this must be balanced against the desirability of reducing the interval during which the incompletely vaccinated individual is exposed to risk. For this reason, the two primary doses should be spaced not less than two weeks apart, and, during periods of potentially high prevalence, two doses should be given within this short interval. In periods, or regions, of low prevalence, a preferable spacing would be four to six weeks, but may be longer. The third dose, in either case, should be given approximately seven months, or longer, after the second dose, and this interval can be prolonged as long as desired or convenient but should be administered prior to the ensuing seasonal prevalence. A third dose, given some seven months after the primary, not only enhances the level of antibody induced by the primary series but affords a third chance for primary sensitization in the event that the responsiveness of the individual, and the relative potency of the vaccine employed, was such as to have failed to result in a primary response to the first or second doses given earlier.

Thus the schedule of inoculation recommended represents a reasonable compromise, within practical limits, that permits the utilization of the benefits to be derived from repeated inoculation. Moreover, the suggested schedule is intended to provide at least three opportunities for inducing primary sensitization, thereby reducing the practical importance of the factor of individual variation in the ease of development of the immune state. Although a wide latitude exists in the intervals over which inoculations may be spaced, in the route for inoculation and in dosage for an effective response, the factors of critical importance are antigenic mass and adequate spacing of inoculations. In respect to the use of small inoculums intradermally, the evidence is clear that this does not result in effects equal to those achieved with larger doses that can be given by percutaneous routes.

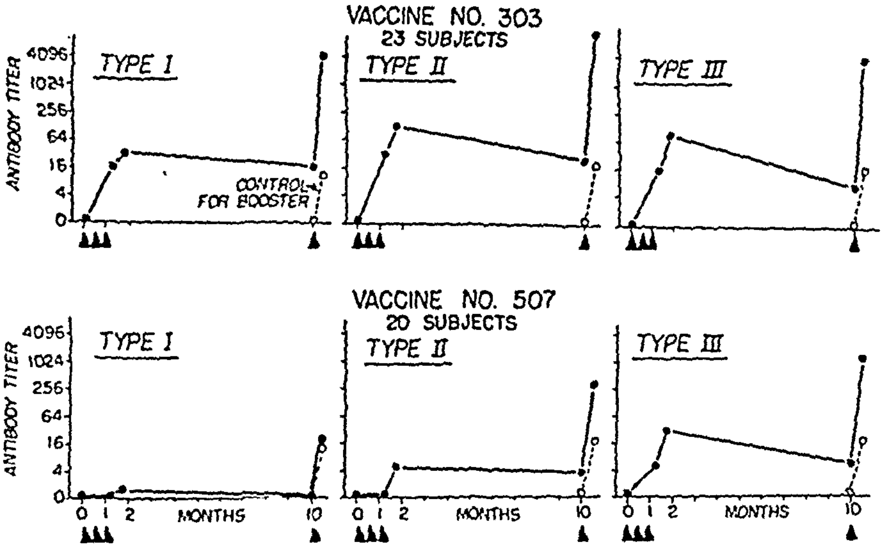

Fig. 12.—Effect of booster dose 10 months after vaccination with two different vaccine lots used in 1954 field tests.

From the evidence at hand, the potency of the vaccine, for each type, could be selected in terms of the effects induced by the different dilutions of reference vaccine A. When vaccines of greater than minimal potency are employed, it should be expected that routine immunization will induce a substantial immunologic effect with a high degree of reliability—even after one dose—and this assurance is increased by a second dose. After the third dose, suitably spaced, the effect should, for practical purposes, be complete. Tests for adequacy of immunizing effect will be continued for the next few years to verify the extent to which this does in fact occur with vaccines of the potencies now available.

The objective of such continued observation is the achievement of a routine of such a degree of consistency that there is built into the immunization procedure a wide "margin of confidence" for effectiveness. Since tests for antigenic potency can be readily made, both in laboratory animals and in children, and since the ultimate requirements for full immunizing effect seem not unrealistic of achievement, it would appear that it is merely a matter of fulfilling these requirements that constitutes the problem that stands between the present and the ultimate elimination of paralytic poliomyelitis. That this can be done, insofar as immunologic measurements can be so interpreted, is suggested by results of tests on children who have received a full course of immunization, with commercially produced vaccine as well as with vaccine produced experimentally.

Although the principal effect of vaccination is to create an immunologic barrier to invasion of the central nervous system, an accessory effect may be the reduction in the degree and duration of virus multiplication at the superficial site of infection. In addition, the establishment of secondary foci of multiplication or excretion might conceivably be prevented, thereby reducing the amount and duration of virus elimination.[13] If hyperimmunization, as tends to occur after secondary stimulation (booster) in those previously vaccinated or previously infected, is influential in creating a state of resistance to infection as well as to the already existent state of resistance to paralysis, then it can be expected that the reservoir of infection will be further reduced.

The concept[17] that some previously infected individuals may be silent reservoirs, serving as intermittent sources of infection, seems to fit best the facts concerning the epidemiologic behavior of this disease. If this be true, then it is conceivable that hyperimmunization, which, if sufficiently great, will limit or prevent the establishment of infection, will also limit or reduce the reservoir of infection by reducing the number, frequency, and duration of carriers in the population. Thus, it could be that vaccination, as it tends to do in other diseases, may bring about a sharper reduction in the amount of paralytic poliomyelitis than is to be expected merely on the basis of the number of individuals vaccinated. That this may well occur is indicated by the reduction, in the summer of 1955, not only in the number of cases of paralytic poliomyelitis but in the number of cases of nonparalytic poliomyelitis in vaccinated as compared with nonvaccinated children, even in those given but one dose of vaccine.[12]

If the mechanism of immunity that has been described is correct, then it is to be expected that the protective effect against paralytic poliomyelitis will be essentially the same during the season immediately following inoculation and during subsequent seasons. This view is based on the indications that, in spite of a tendency for antibody levels to decline, the hyperreactive state appears to persist, and it seems that, through the hyperreactive state, immunity to paralysis may also be mediated. The indications that this mechanism has been operative in vaccinated persons are suggested by the meager evidence that is available that the ratio of cases between vaccinated and controls was essentially unchanged as the 1954 or 1955 seasons progressed, although the tendency for antibody to decline continued during the period in question. Moreover, there has not been any obvious evidence during the summer of 1955 of a reduction in the ratio of effectiveness in those vaccinated in 1954 but not revaccinated in 1955.

Changing epidemiologic patterns will make it difficult to acquire quantitative information on degree of persistence of immunity. Therefore, as a guide to decisions in practice, it is essential to establish and to understand the dynamics both of infection and of immunity in the individual and in the community. The validity of the concepts that have been expressed, of the mechanism of immunity, and of the significance of these concepts will be revealed in time.

Summary

The amount of virus antigen injected is the principal determinant of the intensity of the immune response. This is reflected in the level of antibody induced and/or in the degree of immunologic hyperreactivity effected. Although antibody, at demonstrable levels, tends to persist for long periods, it has also been observed that immunologic hyperreactivity continues, even in those cases in which antibody has declined to nonmeasurable levels. The indications are that immunity to paralysis is mediated not only through existing antibody in the circulating blood but through the mechanism of immunologic hyperreactivity that calls forth antibody sufficiently rapidly, after exposure, to intercept invasion of the central nervous system even though pharyngeal or intestinal infection may have occurred.

This study was aided by a grant from the National Foundation for Infantile Paralysis.

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CLINICAL NOTES

REPORT OF TWO CASES OF CARDIAC TAMPONADE IN UREMIC PERICARDITIS

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and
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Pericarditis is a frequent complication of uremia in both acute and chronic renal failure.[1] The recognition of uremic pericarditis has been important for three reasons: 1. The onset of pericarditis in uremia has been found to have prognostic significance.[2] 2. Pericarditis is frequently the cause of confusing and distressing pain.[3] 3. Electrocardiographic abnormalities occurring late in uremia are often the result of pericarditis.[4]

Two cases of chronic renal failure, which were seen recently in this hospital, have served to illustrate another significant aspect of uremic pericarditis. In both instances the immediate cause of death was cardiac tamponade, which was a complication of uremic pericarditis. Because of the lack of appreciation of tamponade as a complication of uremic pericarditis in textbooks and the literature, it was thought that a report of these cases would be of interest.

Report of Cases

CASE 1.—A 29-year-old man entered the Salt Lake Veterans Administration Hospital for the second time on Feb. 20, 1953, with weakness and anorexia of one month's duration and the complaint of pain of 10 days' duration in the left shoulder and back.

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BUREAU OF MEDICAL ECONOMIC RESEARCH

PHYSICIAN MORTALITY, 1949-1951

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The deaths of 10,738 physicians, 1949 to 1951, relative to a 1950 physician population of 204,450 comprise the basic statistics of this study of physician mortality. Through a detailed examination of these data by age and by cause of death, the highlights of physician mortality experience for the period cited are presented and compared with the mortality experience of white males of the same ages. The presentation of these findings will follow a brief description of the nature of the data and the methods employed in their compilation and development. A more detailed description of the data and methods, along with supplementary tables and the present article, will be presented in Bulletin 103, available from the Bureau of Medical Economic Research, American Medical Association.

Basic Data

The population of 10,738 physician deaths was censused through the use of A. M. A. files and through the procurement of death certificates from state and city departments of health. Without the cooperation of the vital statisticians in these departments, this study would have been impossible. All the deaths were verified by both sources of information except 175 for which death certificates could not be obtained, although these deaths were confirmed by other sources in addition to A. M. A. records. The three-year period during which these deaths occurred was selected for intensive study because it is the most recent for which the National Office of Vital Statistics has tabulated population mortality data for white males, white females, nonwhite males, and nonwhite females.[1]

To be evaluated in terms of mortality experience, the deceased population must be related to its corresponding living population, which is customarily censused on the mid-date of the period under examination. We chose April 1, 1950, for our census of physicians living in the continental United States in order to match the date employed by the National Office of Vital Statistics in computing its life tables. As the result of information received on the death certificates as well as knowledge gained through other checks on the living physician population, a final revised estimate of 204,450 was obtained. In Bureau Bulletin 94, "Distribution of Physicians by Medical Service Areas" (1954), the total was 204,995 for the same date. Both sets of data were derived from the files of the Directory Department, in which almost all the names are those of graduates of approved American and Canadian schools or graduates of other medical schools who were or had been licensed to practice medicine in at least one of the 48 states or the District of Columbia. These refinements of the basic data involving a net reduction of 545 in the living population have, in our opinion, greatly enhanced their quality.

Unfortunately our data on living physicians have two defects. Thus far we have not been able to census the populations of living specialists and so have not examined physician mortality by specialty. We realize, nevertheless, that we are omitting an aspect of physician mortality in which physicians are interested. The second defect is that A. M. A. data do not identify all physicians by sex. Our attempt to determine sex by examining the physician's first name not only resulted in a suspiciously high count of female physicians (10,000) but was proved to be defective; for example, some physicians classified as females by their first names obtained their premedical education in colleges that have never enrolled a female. We were unable, therefore, to determine the population of living female physicians, although we knew the number who died during the three years was 433. It also was not possible to identify physicians by race, although the living nonwhite physicians are known to number between 4,000 and 5,000; very few are females. If the poorer mortality experience of nonwhite males in comparison with white males generally applies also to nonwhite physicians, our inclusion of nonwhite physicians should serve to offset, somewhat at least, the inclusion of females. The extent, however, to which these two compensating factors balance is unknown to us and is recognized as a basic defect in the data. Since 92% of the physicians were white males, white male mortality is used as the basis of comparison in this study.

Valid comparisons between physician and white male mortality experience can be made only when the white male population is adjusted to the age distribution of the physician population. The physician population, unlike the white male population, includes no children. Hence the number dying per thousand could not be used for mortality or cause-of-death comparisons. So 204,450 white males of the same age distribution as the 204,450 physicians is the frame of reference used in this study. Comparisons between these two groups reveal differences in mortality rates only. The procedure commonly employed to make the adjustment is to apply white male death rates by age and by cause to the physician population and to designate the deaths so computed as "expected" deaths, the number that would have occurred among physicians if their mortality experience had been identical to that of white males. Hereafter in this study, unless otherwise indicated, references to white male deaths will be references to these "expected" deaths of a white male population of the same age distribution as the living physician population.

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Age-Specific Mortality

The analysis of physician mortality experience by age includes death rates by five-year age groups, expectation of life at certain ages, and average ages at death for both physicians and white males. Since mortality rates for all causes by single years of age are available in the life tables for white males, our computations of expected deaths were made for each age, 20 and over. They are tabulated by five-year age groups in table 1 for the sake of parallel presentation with the data on deaths by individual causes to be discussed later. The numbers of deaths among white males by individual causes are available only for five-year age groups.

The Bureau's deck of punch cards was used to determine the ages of the living population. These punch cards, developed over a number of years, show only the year of birth, as does the American Medical Directory. Although information on day and month of birth could be found for many physicians in the files of our Directory Department, it was not practical for the purpose of this study alone to use other than the year of birth. The month and day as well as the year of birth were, of course, reported on the death certificates. We assumed that the births of the living population were evenly distributed throughout the calendar year of birth. In order to determine the attained age as of April 1, 1950, a quarter-year adjustment was necessary and accounts for the quarters (demicals) in the age distribution of the living population by five-year age groups in column (2) of table 1. The age of the dying was the age at the last birthday, and no comparable adjustment of a quarter of a year was required.

The physician deaths during the three years 1949-1951 are shown by age groups in column (3) of table 1. The physician death rates in column (5), however, present the number of deaths per thousand in the age groups during a single year. For example, in the age group 20-24, there were 2,719.75 living physicians as of April 1, 1950, and 12 died during the three-year period 1949-1951. Adjusting the deaths to the number for a single year, instead of the number for three years, the mortality rate (number dying per thousand per year) for this age group was 1.47. For the age group 25-29 the living population on the census date numbered 22,689.50; 75 died during the three-year period under examination, making the death rate for one year 1.10.

Actual Versus Expected Deaths

Whether these physician mortality rates are high or low can best be ascertained by comparing them with the experience for white males. If the 2,719.75 physicians in the age group 20-24 had been subjected to white male mortality experience in 1949-1951, 14.2 deaths [column (4), table 1] could have been expected. The resulting mortality rate then in this age group was 1.74 [column (6)], and the percentage of actual physician deaths to expected was 84.5. In contrast to the experience of white males in terms of the deaths they would have experienced at these ages, physician mortality was 15.5% lower. The expected deaths and the percentage of actual to expected deaths [column (7)] for the five-year age groups are presented in table 1.

Table 1.—*Physician Population as of April, 1950, Deaths and Death Rates, 1949-1951, of Physicians and White Males of the Same Ages, and Percentage of Actual to Expected Deaths*

Age Group (1)	Physician Population, 4/1/50 (2)	Physician Deaths, 1949-1951 (3)	Expected Deaths of White Males, 1949-1951 (4)	Physician Death Rates (5)	White Male Death Rates (6)	Percentage of Actual to Expected Deaths (7)
20-24	2,719.75	12	14.2	1.47	1.74	84.5
25-29	22,689.50	75	116.7	1.10	1.71	64.3
30-34	25,155.75	120	154.2	1.59	2.04	77.8
35-39	27,790.00	165	248.3	1.98	2.98	66.5
40-44	26,706.25	328	383.6	4.09	4.79	85.5
45-49	20,906.25	448	484.9	7.14	7.73	92.4
50-54	17,364.00	599	636.2	11.50	12.21	94.2
55-59	14,372.25	751	819.7	17.42	19.01	91.6
60-64	13,039.00	1,130	1,099.8	28.89	28.12	102.7
65-69	11,742.50	1,458	1,441.1	41.39	40.91	101.2
70-74	10,210.25	1,834	1,857.2	59.87	60.63	98.8
75-79	6,808.75	1,680	1,852.1	82.25	90.67	90.7
80-84	3,447.00	1,268	1,351.5	122.62	133.59	91.8
85-89	1,120.25	580	679.0	172.58	202.04	85.4
90-94	320.00	240	274.9	250.00	286.35	87.3
95-99	54.75	45	64.8	273.97	394.52	69.4
100 and over	3.75	5	5.6	444.44	497.78	89.3
Total	204,450.00	10,738	11,513.8	17.51	18.77	93.3

Whereas 10,738 physicians died during this three-year period, the number of expected deaths would have been 11,513.8. The percentage of actual to expected deaths, therefore, for the entire population was 93.3. The fact that physician deaths were 6.7% fewer than the number that white males of the same ages would have experienced indicates that physician mortality for these three years was definitely lower than that of all white males. (The percentage of actual to expected deaths was 94.7 for a hypothetical white population of 95% males and 5% females at each age, a very rough allowance for our inability to exclude females.) The ratio of actual to expected deaths was lowest for the age group 25-29 (64.3%) and highest for the age groups 60-64 (102.7%) and 65-69 (101.2%). As will be noted later in the discussion of causes of death, the excess mortality of physicians in these two age groups, 60-64 and 65-69, was probably a result of the excess number of physician deaths from diseases of the heart.

Other Comparisons

The complete life table for physicians, together with an account of its computation, will be presented in Bulletin 103; it records the expectation of life for physicians at various ages according to their 1949-

1951 mortality experience. At the start of their careers, physicians have approximately 45 years of life ahead of them. More specifically, the average number of years remaining for physicians according to their 1949-1951 experience was 45.9 at age 25, 44.9 at 26, 36.3 at 35, 23.3 at 50, and 13.0 at 65. The percentage of those alive at selected ages who will reach 70, according to this same experience, was 56.2 for those age 25, 56.8 for those 35, and 58.6 for those 50. Consistent, moreover, with our findings regarding the relationship of actual to expected deaths at various ages, the life table values show a higher expectation of life for physicians than white males at all ages (25 to 102). The smallest difference in life expectancies under age 85 between the two groups was only 0.1 year at age 60, while the greatest was 0.9 year at age 25.

The average ages at death differ little between the two groups. The median age at death for physicians was lower (70.8 versus 71.0 years) but the mean age at death for physicians was higher (68.6 versus 68.4 years). These differences, involving data by five-year age groups, were not statistically significant.

Mortality by Cause

For our analysis of physician deaths by cause, we classified the deaths into 11 groups of leading causes and a residual group, "all other causes." The cause of death categories are defined by using the grouping and code numbers in the Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death, sixth revision, World Health Organization, 1948. In our study, causes of death were grouped as follows:

1. *Diseases of the Heart* (401, 402.1, 410-443). This group includes rheumatic fever with heart involvement, chorea with heart involvement, chronic rheumatic heart disease, arteriosclerotic and degenerative heart disease including diseases of the coronary arteries, hypertensive heart disease, and other diseases of the heart.
2. *Malignant Neoplasms* (140-205). This group includes all malignant neoplasms classified according to site as well as neoplasms of the lymphatic and hematopoietic tissues. It excludes benign and unspecified neoplasms.
3. *Vascular Lesions Affecting the Central Nervous System* (330-334). This group includes subarachnoid and cerebral hemorrhage, cerebral embolism and thrombosis, and other and ill-defined vascular lesions affecting the central nervous system. It excludes intracranial lesions due to trauma and any condition specified as a late effect, sequela, or death one year or more after onset.
4. *Accidents* (E800-E962). This group includes all transport accidents, accidental poisoning, falls, and other accidental deaths.
5. *Nephritis and Nephrosis* (590-594). This group includes acute, chronic, and unspecified nephritis, nephrosis, and other renal sclerosis.
6. *Influenza and Pneumonia* (480-483, 490-493).
7. *Tuberculosis* (001-019). This group includes all forms of tuberculosis.
8. *Diabetes Mellitus* (260).
9. *General Arteriosclerosis* (450). This group excludes arteriosclerosis with hypertension, and other diseases involving arteriosclerosis.
10. *Cirrhosis of Liver* (581). This group includes cirrhosis of liver with and without mention of alcohol or alcolohism.
11. *Suicide* (E963, E970-E979). This group includes deaths from nonaccidental self-inflicted injuries in suicide or attempted suicide, and excludes accidental self-inflicted injuries.
12. *All Other Deaths.* Our category of "all others" includes deaths from all causes not included in the above major groups.

The number of physician deaths by cause involves decimals as a result of the distribution among the 12 categories of the 175 deaths for which death certificates could not be obtained and for which cause of death was unknown. Only one-sixth of the 10,563 death certificates indicated that autopsies had been performed. We are unable to measure the influence, if any, on our data of better certification of physician deaths. The total number of physician deaths for each leading cause is shown in column (2) of table 2. In order to compare them with the total number of white male deaths, we developed white male death rates by five-year age groups for 1949-1951 from data published by the National Office of Vital Statistics.[2] The procedures employed are described in Bulletin 103. Despite our efforts to match the data used by the National Office of Vital Statistics in computing the life tables, a small discrepancy appears between the total number of expected deaths for all ages by individual causes and the total number of expected deaths for all causes computed for each year of age. The difference is only 16, or 0.1%; this difference would increase the percentage of actual to expected deaths from 93.3 to 93.4. It can be attributed to the smoothing of raw data involved in computing the life tables.

As discovered in earlier studies, we found that by far the largest number of deaths among physicians (and among the general population) were due to diseases of the heart, which accounted for 5,265.6 physician deaths, or 49.0% of the total, and 5,103.3, or 44.4%, of the expected deaths among white males of the same ages. Malignant neoplasms (1,503.9 deaths or 14.3%), vascular lesions affecting the central nervous system (1,201.7 deaths or 11.2%), and accidents (488.6 deaths or 4.6%) ranked second, third, and fourth in the number of deaths for physicians; these three causes also ranked second, third, and fourth for white males. The four leading causes together accounted for 79.0% of physician deaths compared to 75.3% of white male deaths. Each of the remaining causes accounted for only 1.1 to 2.6% of the total deaths. The cardiovascular-renal diseases (groups 1, 3, 5, and 9) accounted for 63.4 and 59.6% of physician and white male deaths respectively. These data and those for the other causes of death are presented in table 2.

Ratio of Actual to Expected Deaths by Cause

The ratio of actual to expected deaths by cause provides a comparison of physician and white male experience that, as in the case of mortality rates above, renders these data more meaningful. These comparisons are shown in table 2. For only three causes—diseases of the heart, diabetes mellitus, and suicide—was there a greater number of deaths than would have been expected in a white male population of the same ages; the percentages of actual to expected deaths were 103.2, 135.1, and 102.8. For each of the eight other causes, mortality experience among physicians in 1949-1951 was more favorable than among white males. In terms of the percentage of actual to expected deaths, physician mortality experience compared most favorably for tuberculosis (119.1 physician deaths), 46.6%, and influenza and pneumonia (160.7 physician deaths), 53.8%. In contrast, the least favorable experience appears to be that for diabetes mellitus (202 physician deaths), with 135.1% of expected deaths.

The difference between the number of physician deaths and the expected number was substantial for a few of the causes. How great a difference is required in order to justify the assertion that mortality among physicians from the named cause of death was significantly different from the mortality among white males? In applying the tests of significance to the differences, we recognize that there is room for more than one opinion. The standard deviation, in percentage, of the ratio of actual to expected deaths from each cause, in percentage, is set forth in column (5) of table 2. Consider the difference for diseases of the heart. Was the 3.2% excess of physician deaths great enough in relation to the standard deviation, 1.4% (1.42), to conclude that mortality from diseases of the heart among physicians was significantly higher than among white males and could not reasonably be attributed to mere chance? The difference is more than twice the standard deviation and almost 2.32 standard deviations, the required difference for 99 chances out of 100—single tail of the normal curve. The difference is also more than 1.64 standard deviations, the required difference for 95 chances out of 100. Those who believe that the difference must be at least 2.32 standard deviations will conclude that the difference in mortality from diseases of the heart among physicians and white males was not quite statistically significant. Those who consider 95 chances out of 100 a sufficient confidence level will contend that the difference in mortality from diseases of the heart among physicians and white males was clearly statistically significant. We conclude that, on balance, physician mortality from diseases of the heart was significantly higher than among white males.

TABLE 2.—*Number and Percentage of Physician and of White Male Deaths, and Ratio of Actual to Expected Deaths, By Cause, 1949-1951*

Cause of Death	Physician Deaths		Expected Deaths of White Males		Percentage of Actual to Expected Deaths	Standard Deviation,* %
	No.	%	No.	%		
(1)	(2)	(2a)	(3)	(3a)	(4)	(5)
1. Diseases of the heart	5,265.6	49.04	5,103.3	44.39	103.2	1.4
2. Malignant neoplasms	1,530.9	14.26	1,649.4	14.35	92.8	2.4
3. Vascular lesions of the central nervous system	1,201.7	11.19	1,247.6	10.85	96.3	2.8
4. Accidents	488.6	4.55	660.6	5.75	74.0	3.3
5. General arteriosclerosis	207.8	1.93	298.4	2.59	69.6	4.8
6. Diabetes mellitus	202.0	1.88	149.5	1.30	135.1	9.5
7. Suicide	190.8	1.78	185.6	1.61	102.8	7.4
8. Influenza and pneumonia	160.7	1.50	298.8	2.60	53.8	4.2
9. Nephritis and nephrosis	131.3	1.22	199.7	1.74	65.7	5.7
10. Cirrhosis of the liver	120.2	1.12	137.2	1.19	87.6	8.0
11. Tuberculosis, all forms	119.1	1.11	255.8	2.22	46.6	4.3
12. All other causes	1,119.3	10.42	1,311.8	11.41	85.3	2.6
Total	10,738.0	100.00	11,497.7	100.00	93.4	0.9

* The standard deviation is the percentage of actual to expected deaths, as shown in column (4), divided by the square root of the actual number of deaths among physicians as shown in column (2). This formula was suggested by Edward A. Lew, Statistician, Metropolitan Life Insurance Company. See also page 11, Impairment Study, 1951, Society of Actuaries, Chicago.

For the other causes of death a choice between 95 chances out of 100 and 99 chances out of 100 is not required. According to the test of 95 chances out of 100—and, of course, 99 out of 100—the differences in mortality among physicians and white males was not significant for vascular lesions affecting the central nervous system, suicide, and cirrhosis of the liver. We conclude, therefore, that the differences noted in the number of deaths and in the ratio of actual to expected deaths among physicians and among white males from these three causes were too small to exclude the possibility that they resulted from mere chance. On the other hand, the differences in mortality between physicians and white males were significant for malignant neoplasms, accidents, general arteriosclerosis, diabetes mellitus, influenza and pneumonia, nephritis and nephrosis, and tuberculosis by the test of 99 chances out of 100. Most important of all, the difference of 6.6 percentage points (100% minus 93.4%) between the mortality of physicians and white males from all causes combined was definitely statistically significant by the test of 99 chances out of 100.

Although diabetes mellitus was a cause for which there were proportionately more physician than expected deaths, it accounted for only 202, or 1.9%, of all physician deaths; the number of expected deaths was only 149.5. The excess, 52.5, was concentrated at the older ages; at ages 60 and over the excess was 54.5, but below age 60 the expected deaths were 2 more than the actual. This fact suggests, but does not prove, greater success by physicians as compared with white males in postponing death from diabetes. Unfortunately, the case rate incidence by age groups for the two populations is not known. The unfavorable experience of physicians from diseases of the heart likewise was concentrated among certain age groups; virtually all the excess deaths, 162.3, occurred at ages 40-74, with approximately 65% of them at ages 60-74.

Other Measures for Evaluating Leading Causes

Further evaluation of the relative importance of the leading causes of death can be made by the use of two additional measures. Rank by numbers of deaths has been employed up to this point in the examination of the ratio of actual to expected deaths. The other two measures are number of life years lost and number of working years lost due to the several causes respectively. In 1949-1951, 10,738 physician deaths, as shown in table 3, resulted in the loss of 132,439 years of life and 39,014 years of working life. Correspondingly, the 11,497.7 expected deaths among white males of the same ages resulted in the loss of 141,791 life years and 45,756 *working life years. These measures* were originally discussed in Bureau Bulletin 64,[3] and their computation for this study will be explained and presented in Bulletin 103.

Life years lost, as a measure of the force of death, impresses upon us forcefully what the loss of life involves. It takes into consideration the age at which the person died and the years he would have lived according to the expectation of life for a person at that age. Such a measure clearly gives added weight to the impact of deaths from those causes that strike the younger members of the population. Working years lost as a related measure attaches even greater weight to the youthfulness of the dying. Being more concerned with the economically productive years of life rather than the whole of life, it additionally minimizes the effect upon the nation's output of goods and services of those deaths from causes whose impact occurs chiefly after age 65. We assigned this age as the terminal point of a person's productive years, although the productive period ends before age 65 for some and after age 65 for others. Accordingly, working life expectancy at ages 65 or over is zero; the years "to be lived after age 65" are excluded in computing working life expectancy, the factor by which the number dying each year under age 65 is multiplied. Comparative data based on age 70, which some may consider a more realistic terminal age, will be presented in Bulletin 103. It should be realized that the higher we designate the terminal productive year, the closer working years lost approximates total life years lost. By designating 65 as this age, we reveal more forcefully which of the causes of death is least severe in inhibiting the potential for production.

In dealing with the physician population and white male experience adjusted to such a population, we must realize that we are considering an adult population. The differences between the ranking by numbers of deaths and those revealed by life years lost and working years lost among such a population would be even more pronounced among a population covering all of the years of life.[3] For convenience, the rankings of the top five leading causes according to the three measures are presented in table 3A, first for physicians and then for white males of the same ages. For physicians, diseases of the heart and malignant neoplasms ranked first and second by all three measures. Vascular lesions affecting the central nervous system ranked third by number and by life years lost, but only fifth by working years lost. Accidents ranked fourth, fourth, and third, whereas suicide ranked seventh, fifth, and fourth. For white males of the same ages, diseases of the heart rank first according to the three measures but accidents displaced malignant neoplasms in second position according to working years lost. Vascular lesions affecting the central nervous system ranked third, fourth, and sixth. Accidents ranked fourth, third, and second; and tuberculosis ranked seventh, fifth, and fourth.

TABLE 3.—*Ranking of Eleven Groups of Leading Causes of Deaths, 1949-1951, of Physicians and of White Males of the Same Ages by Three Measures: Number of Deaths, Life Years Lost, and Working Years Lost*

Cause of Death	No. of Deaths			Life Years Lost			Working Years Lost		
(1)	No. (2)	% (3)	Rank (4)	Years (5)	% (6)	*Rank* (7)	Years (8)	% (9)	*Rank* (10)
					A. Physicians				
1. *Diseases of the heart*	5,265.6	49.04	1	*63,033.4*	*47.60*	1	16,356.2	41.92	1
2. Malignant neoplasms	1,530.9	14.26	2	18,565.4	14.02	2	4,903.1	*12.57*	2
3. Vascular lesions of the central *nervous system*	1,201.7	11.19	3	*11,770.0*	*8.89*	3	1,965.2	5.04	5
4. *Accidents*	488.6	4.55	4	9,051.3	6.83	4	4,824.6	12.37	3
5. General arteriosclerosis	207.8	1.93	5	1,320.4	1.00	11	28.5	.07	11
6. Diabetes mellitus	202.0	1.88	6	2,212.4	1.67	6	451.6	1.16	9
7. *Suicide*	190.8	1.78	7	*4,455.4*	*3.36*	5	2,648.8	6.79	4
8. *Influenza* and pneumonia	160.7	1.50	8	1,575.1	1.19	10	385.9	.99	10
9. Nephritis and nephrosis	131.3	1.22	9	1,620.6	1.22	9	484.9	1.24	8
10. Cirrhosis of the liver	120.2	1.12	*10*	*1,822.2*	*1.38*	8	666.8	1.71	7
11. Tuberculosis, all forms	119.1	1.11	11	*1,974.9*	*1.49*	7	848.2	2.17	6
12. All other causes	1,119.3	10.42	...	15,037.6	11.35	...	5,449.9	13.97	...
Total	10,738.0	100.00		132,438.7	100.00		39,013.7	100.00	
					B. White Males				
1. Diseases of the heart	5,103.3	41.39	1	57,682.2	40.68	1	15,050.1	32.89	1
2. *Malignant neoplasms*	1,649.4	14.35	2	20,635.8	14.55	2	6,080.9	13.29	3
3. *Vascular* lesions of the central nervous system	1,247.6	10.85	3	11,785.6	8.31	4	2,060.4	4.50	6
4. Accidents	660.6	5.75	4	13,659.4	9.63	3	7,963.4	17.40	2
5. General arteriosclerosis	298.4	2.59	6	1,891.9	1.34	10	79.3	.17	11
6. *Diabetes mellitus*	149.5	1.30	10	1,780.4	1.26	11	484.9	1.06	10
7. *Suicide*	185.6	1.61	9	3,831.2	2.70	6	2,102.5	4.60	5
8. Influenza and pneumonia	298.8	2.60	5	3,200.4	2.26	7	923.7	2.02	8
9. Nephritis and nephrosis	199.7	1.74	8	2,509.6	1.77	8	907.9	1.99	9
10. Cirrhosis of the liver	137.2	1.19	11	2,389.1	1.69	9	1,088.8	2.38	7
11. Tuberculosis, all forms	255.8	2.22	7	4,895.8	3.45	5	2,475.7	5.41	4
12. All other causes	1,311.8	11.41	...	*17,529.4*	12.36	...	6,538.7	14.29	...
Total	11,497.7	100.00		141,790.8	100.00		45,756.3	100.00	

Changes in rank as between numbers of deaths and life years lost reflect the added weight given by the latter measure to deaths at earlier ages; changes in rank as between life years lost and working years lost reflect the zero weight given by the latter to deaths at age 65 and over. Higher rank—rank one is highest—for a cause of death according to life years lost and even more so according to working years lost reveals that its incidence is relatively high at the younger ages of life In this manner we can explain the rise in rank for accidents, tuberculosis, and suicides and the fall in rank for vascular lesions affecting the central nervous system and the decline in the percentage importance of diseases of the heart.

These observations apply with the same force to the lesser causes of death as to the major. Among them we find for physicians that not only suicide but also tuberculosis and cirrhosis of the liver shift to a higher rank in life years lost than in mere numbers of deaths, and, as between life years and working years lost, nephritis also moves up in rank. Conversely, general arteriosclerosis and pneumonia shift downward respectively to the last and next to the last positions for both life and working years lost. Even diabetes mellitus drops from sixth in numbers and life years lost to ninth in working years lost. Since the extra deaths among physicians from diabetes mellitus occurred at ages 60 and over, it is not surprising that white males lost a greater number of working years from diabetes mellitus than did physicians. The direction of movement in rank among causes so far as these measures are concerned was the same for white males as for physicians with but two exceptions: for physicians nephritis was higher and diabetes lower in working years lost than in life years lost, but the shifts were just the opposite for white males.

TABLE 3A.—*Ranking of Five Leading Causes of Death for Physicians and White Males*

Cause of Death	By No of Deaths	By Life Years Lost	By Working Years Lost
A Physicians			
Diseases of the heart	1	1	1
Malignant neoplasms	2	2	2
Vascular lesions	3	3	5
Accidents	4	4	3
Suicide	7	5	4
B White Males of the Same Ages			
Diseases of the heart	1	1	1
Malignant neoplasms	2	2	3
Vascular lesions	3	4	6
Accidents	4	3	2
Tuberculosis	7	5	4

The relative positions of the causes as between physicians and white males were changed little in shifting from one measure to another It is true that accidents moved ahead of malignant neoplasms for white males in working years lost and general arteriosclerosis fell to last place for physicians in life years lost. The higher rank for suicide and diabetes among physicians than white males, however, prevailed for all three measures, just as the higher rank for pneumonia and tuberculosis did among white males. Moreover, diseases of the heart and malignant neoplasms in this adult population accounted for almost the same percentages of totals according to all three measures

Some Historical Comparisons

The death rates for 10-year age groups (age 25 and over) developed by Emerson and Hughes[4] for 1925, applied to our age distribution of living physicians in 1950, produce 12,842 deaths, or 16 5% more than the reported total of 10,726 (excluding 12 deaths below age 25) in 1949-1951. Similar computations with the age-specific rates for 10-year age groups developed by Dublin and Spiegelman[5] for 1938-1942 produce 12,394 deaths, or 13 5% in excess of the 10,726 deaths in 1949-1951. These differences roughly measure the improvement in physician mortality since 1925.

Using the age-specific mortality rates among white males for 1920 applied to the age distribution of white male physicians in 1925, Emerson and Hughes found an excess in the number of deaths among white males. For the period 1938-1942, Dublin and Spiegelman found that the number of deaths among male physicians slightly exceeded the number of deaths expected among white males of the same ages. Our present study for 1949-1951, like the 1925 study and unlike the 1938-1942 study, found an excess in the number of deaths among white males of the same ages as our physician population. The differences in techniques and our belief that our source data are superior to those in the two preceding studies of physician mortality make us hesitant to conclude that the relationship between the number of physician deaths and the number of deaths among white males of the same ages has undergone any substantial change since 1925 or since 1940.

Moreover, age-specific mortality rates for white male physicians were lower than those for white males in 1925, and slightly higher (for male physicians) in 1938-1942, as already noted in this study, the rates (for all physicians) were slightly lower in 1949-1951. Physician death rates in these three studies have compared most favorably with those of white males at the younger ages (25-34 and 25-44) and least favorably within the broad age group 45-64. For the most recent period examined, 1949-1951, we found the physician experience poorer than that for white males at ages 60-69 Certain other comparisons for these two previous studies are suggestive but not conclusive.

Experience with respect to expectation of life is similar to that for death rates. For physicians the expectation of life at age 30 rose from 38 0 years in 1925[6] to 41.0 years in 1950, for white males the corresponding average number of years of life remaining were 37 6 and 40 3. The physician at age 50 had on the average 21.7 years remaining in 1925 and 23 2 in 1950, white males had 21.7 in 1925 and 22 8 in 1950 More generally, physician expectation of life was lower than that of white males in 1925 at the ages over 50, and in 1938-1942 between the ages of 25 and 70, and the excess for physicians was least in 1949-1951 at age 60.

Unfortunately, groupings of physician deaths by causes for the purpose of comparing our study with the two previous studies is hazardous because of revisions in the international list of the causes of deaths that were made between 1925 and 1940 and between 1940 and 1950. We made a considerable number of computations for the purpose of producing such historical comparisons by groups of causes The comparisons did indicate that in 1938-1942 there were several groups of causes for which physician deaths exceeded expected deaths among white males of the same ages, whereas in 1949-1951 there were only three such causes.

Summary

An examination of the death certificates of more than 10,000 physicians who died during the period 1949-1951 in relation to the population of living physicians as of April 1, 1950, revealed that the number of physician deaths was only 93 3% of the number of deaths that would have been expected if physicians had experienced the age-specific mortality rates of white males. Physician mortality experience was better than that for white males in all except two of the five-year age groups and for 8 of the 11 groups of leading causes. It was poorer in the age groups 60-64 and 65-69 and for diseases of the heart, diabetes mellitus, and suicide; for the first two of these three causes, the differences were statistically significant. Although the expectation of life at all ages was greater for physicians than for white males, differences in the median and mean ages at death were not significant. Diseases of the heart clearly comprised the leading cause of death for both physicians and white males according to all three measures—numbers of deaths, life years lost, and working years lost. Unfortunately, separate mortality tables could not be developed for the several speciality groups and for females.

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COUNCIL ON FOODS AND NUTRITION

Report to the Council

The following comments on fats in the diet are based on a speech given at the Margarine All-Industry Conference, Hot Springs, Va., May 24, 1956. The Council has authorized publication of this report.

PHILIP L. WHITE, SC.D., *Secretary.*

FATS IN THE DIET IN RELATION TO ARTERIOSCLEROSIS

Charles D. May, M.D., Iowa City

Current research on the causes of arteriosclerosis and coronary heart disease at least encourages an optimistic outlook. Recent findings indicate that these conditions may be acquired diseases rather than inevitable consequences of the aging process. Considerable evidence is being accumulated that these conditions, which are most common in some of the more highly civilized populations and appear to be increasing in prevalence, may be in large measure a result of faulty nutrition. A spirit of hopefulness has been aroused that this scourge may be prevented or checked by appropriate regulation of the diet.

It is imperative that the urgency in the situation not be allowed to disrupt a sound and orderly attack on the problem, through exploitation by selfish interests or undue emotion and competitiveness among investigators. A prime need is for conservative, deliberate, and cautious interpretation and application of the fragments of knowledge seemingly related to the solution of these problems. When knowledge seems sufficiently certain to justify application, great caution must be exercised in manipulating the diets of populations lest unanticipated deficiencies or imbalances are created. Interesting but unproved leads must not be made the basis of dietary recommendations.

The focal point of interest at present is the role of dietary fat. Dietary fat is not a single, simple substance but is a complex mixture of fats, steroids, lipid-soluble pigments, and other substances. Some of the fatty acids are essential for certain animals and possibly for the health of the human species and should be supplied in the diet. A certain amount of fat in the diet is required to make it palatable and satisfying. Fats from the various animal and vegetable sources differ in their composition. Nutritionally, a major recognized difference is the relative amounts of so-called essential fatty acids.

For some time there have been indications that the total amount of fat consumed bears some relation to the amount of a fatty substance, cholesterol, that accumulates in the blood. In turn, the cholesterol in the blood has been thought to have some part in the causation of arteriosclerosis and coronary heart disease. High levels of fat in the diet and high levels of cholesterol in the blood have commonly been held responsible for the increasing incidence of these conditions in certain populations that habitually consume diets containing an abundance of fat.

In this connection, it now appears that a distinction must be made between fats from the usual animal sources and the majority of fats of vegetable origin. Recent studies in man and in experimental animals suggest that saturated fatty acids may lead to greater accumulation of cholesterol in the blood than a corresponding amount of unsaturated fatty acids. Unprocessed vegetable fats include larger amounts of the so-called essential unsaturated fatty acids than do most animal fats; the significance of this difference in preventing or relieving the accumulation of excessive amounts of cholesterol in the blood is the subject of intensive investigation at present.

Attention should be focused on the amounts of saturated and unsaturated fats in the diet rather than on the total amounts of fats, whether of vegetable or animal origin. The ratio between the amounts of "essential" unsaturated fatty acids and the saturated fatty

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Chairman, Department of Pediatrics, College of Medicine, State University of Iowa.

acids may be the crucial consideration. An actual deficiency of the so-called essential unsaturated fatty acids severe enough to cause the signs and symptoms observed in animals, but not in man, may not be prevalent; however a relative insufficiency of "essential" unsaturated fatty acids may be important in the pathogenesis of arteriosclerosis. The metabolism of the load of saturated fatty acids imposed by the more abundant fat in the diets of some populations may require the simultaneous provision of larger amounts of "essential" unsaturated fatty acids than are required to deal with diets containing relatively small amounts of saturated fatty acids, whether of animal or vegetable origin.

Besides fat, many other factors such as sex, heredity, age, physical activity, other dietary deficiencies, total amount of calories ingested, and disorders of the liver and kidney influence the amount of cholesterol in the blood. It is not likely that a single cause will be found responsible for all cases of arteriosclerosis, nor should expectation be aroused that this condition will be completely prevented or regularly checked by a mere altering of the kind or amount of fat in the diet. The extent to which the findings in experimental animals can be applied to the disease state in man is by no means certain.

It is easy to assume that obesity is the result of eating too much fat, but this is not strictly true. The body is able to convert other foodstuffs such as carbohydrate into fat. The ingestion of an excessive amount of calories or energy-producing food leads to obesity. It is generally easier and safer for a person to reduce his weight on a diet containing the usual proportion of fat but restricted in total calories because the appetite is better satisfied with a diet containing fat. The problem of obesity is separate from the determination of the proper use of fat in the diet for the promotion of sound nutrition.

The need for caution in setting arbitrary levels for the amounts of animal or vegetable fats in the diet is made apparent when one considers the paucity of pertinent knowledge on the role of fat and the constituent variety of fatty acids in human nutrition. It is obviously unwise and unnecessary to exclude fats from the diet, and even if desirable would no doubt be virtually impossible. Estimations of total fat consumed by populations with differing incidences of arteriosclerosis are too crude to serve as more than a guide for planned investigations. Only a clue as to the qualitative and quantitative significance of unsaturated versus saturated fatty acids has been gained from epidemiological surveys.

The present situation demands that the public receive guidance from competent physicians in the interpretation of the exciting but fragmentary knowledge that seems to bear upon the problems of arteriosclerosis and coronary heart disease. Exploitation of incomplete knowledge by industries for the purpose of competition or by investigators for personal recognition would be irresponsible and detrimental to progress in conquering these major afflictions. Everyone concerned will benefit from any aid that can be given to research directed at basic knowledge of these diseases or to predisposing disturbances in metabolism within the individual, even though the immediate application may not be apparent.

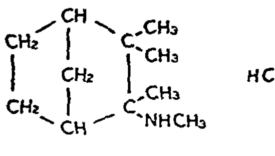
COUNCIL ON PHARMACY AND CHEMISTRY

NEW AND NONOFFICIAL REMEDIES

Monographs and supplemental statements on drugs described here and in subsequent editions of New and Nonofficial Remedies are based on the evaluation of available scientific data and reports of investigations. Applicable commercial names for preparations of evaluated drugs are listed at the end of monographs and parenthetically in the text of supplemental statements; additional commercial names of which the Council is informed will be included with subsequently published supplemental statements and annual editions of New and Nonofficial Remedies.

H. D. Kautz, M.D., *Secretary.*

Mecamylamine Hydrochloride.—3-Methylaminoisocamphane hydrochloride.—The structural formula of mecamylamine hydrochloride may be represented as follows:



Actions and Uses.—Mecamylamine hydrochloride, a secondary amine, exerts a powerful inhibitory effect on the transmission of impulses at autonomic ganglions. Although it is not a quaternary ammonium compound, its ganglionic blocking action is almost identical to that of hexamethonium; therefore, the drug effects a decrease in blood pressure in both normotensive and hypertensive subjects. Unlike hexamethonium, mecamylamine hydrochloride is almost completely absorbed from the gastrointestinal tract and is effective by the oral route. Because it is more uniformly absorbed than hexamethonium, fluctuations in gastrointestinal activity, such as diarrhea and constipation, do not produce so great a variation in hypotensive effectiveness with oral dosage. The drug exerts a longer duration of action than does hexamethonium, and equivalent reduction in blood pressure may be achieved with a lower dose. Since the onset of action is more gradual than that with hexamethonium, the incidence of sudden drops in blood pressure is appreciably reduced. As with all ganglionic blocking agents, prolonged administration leads to decreased effectiveness. This tolerance is not as pronounced with mecamylamine as with hexamethonium and is somewhat less than that observed after therapy with pentolinium tartrate. Cross tolerance between mecamylamine and the other ganglionic blocking agents has not been observed.

In general, the indications for therapy with mecamylamine hydrochloride are the same as those for other ganglionic blocking agents. Thus, the drug may be employed for the treatment of moderate to severe hypertension; it is sometimes successful in arresting the malignant phase of hypertension. Because of the unpleasant nature of side-effects that frequently accompany therapy with ganglionic blocking agents, the use of mecamylamine should generally be reserved for those patients with the more severe forms of hypertension who have not responded adequately to milder drugs such as the Rauwolfia alkaloids. It should never be used in patients with mild or labile hypertension. When employed under carefully controlled conditions with adequate attention to proper regulation of dosage, mecamylamine may be expected to reduce blood pressure effectively and to ameliorate various manifestations of hypertensive-cardiovascular disease. These include such symptoms as headache, dizziness and vertigo, hypertensive encephalopathy and cerebral or subarachnoid hemorrhage, retinopathy, cardiac hypertrophy, and, in some cases, cardiac decompensation. Although the drug may be of benefit in some hypertensive patients with angina pectoris, care should be exercised in its administration, since in other patients it may exacerbate anginal attacks or precipitate myocardial infarction in the presence of coronary insufficiency.

For the treatment of the more severe types of hypertension, mecamylamine can be employed in conjunction with reserpine. Such combination therapy may sometimes produce a more intense antihypertensive effect than can be obtained with mecamylamine alone. In addition, this regimen allows for a lower total dosage of mecamylamine, with a consequent lessening in the side-effects attributable to ganglionic blockade.

Like all agents of this class, mecamylamine hydrochloride is capable of producing a variety of unpleasant side-effects referable to inhibition of both sympathetic and parasympathetic nervous systems. Dryness of the mouth, visual disturbances, constipation preceded by diarrhea, urinary retention, anorexia, nausea and vomiting, weakness and fatigue, sedation, interference with sex functions, dizziness, syncope, and paresthesias have been observed in patients undergoing therapy with this drug. Patients should likewise be warned about the occurrence of orthostatic (postural) hypotension. Extreme care must be exercised with regard to bowel function, since the constipation that frequently accompanies therapy with mecamylamine can proceed into paralytic ileus. To avoid this serious complication, some physicians advise routine concomitant administration of laxatives; however, all patients should be advised to discontinue hypotensive therapy immediately if abdominal distention, decreased borborygmi, or other signs of bowel stasis become evident. In such cases, intensive cathartic therapy is indicated; cholinergic agents, such as neostigmine methylsulfate or bethanechol chloride, may be used to treat impending or frank ileus and urinary retention. In poor-risk patients with malignant hypertension and azotemia or other signs of renal insufficiency, often in association with cerebral atherosclerosis, the administration of large doses may rarely produce tremor or mental aberrations, such as delusions or hallucinations.

Mecamylamine hydrochloride has not been studied for sufficiently long periods to determine with certainty the frequency and severity of all side-effects as compared with those of other ganglionic blocking agents. On the basis of current evidence, it would appear that these are no more troublesome than those with other agents of this class and that some reactions, notably impairment of vision, are less in number and severity than those caused by hexamethonium.

Contraindications to the use of mecamylamine hydrochloride are the same as those for other ganglionic blocking agents. These include such conditions as severe coronary insufficiency, recent myocardial infarction, retinal and cerebral thrombosis, and any other disorder characterized by severe reduction of blood flow to a vital organ. The drug should be administered with caution to patients with renal insufficiency. Rapid, excessive reduction in blood pressure is also dangerous in patients with severe and generalized atherosclerosis. If necessary, pressor amines may be administered to combat excessive hypotensive effects; however, since many patients under therapy with ganglionic blocking agents are more reactive than normal to pressor amines, dosage must be reduced accordingly. Since the drug blocks the normal vasoconstrictor hemostatic mechanisms, its use is contraindicated in any situation in which there is a large reduction in blood volume. Mecamylamine hydrochloride is contraindicated also in the presence of glaucoma, organic pyloric stenosis, and uremia.

Dosage.—Mecamylamine hydrochloride is administered orally. Dosage is highly individualized according to the severity of the hypertension and the response of the patient. The latter varies greatly. Ideally, dosage should be adjusted to the point where desired blood pressure can be maintained without the appearance of severe side-effects. This situation is not always easily attainable. In addition to great variations in individual susceptibility, other factors, such as excessive heat, fever, infection, hemorrhage, pregnancy, antihypertensive or other drugs, alcohol, vigorous exercise, surgery, and anesthesia, alter the hypotensive response. Excessive salt loss, such as that occurring after diarrhea, vomiting, and mercurial diuresis, increases the hypotensive effect of the drug and necessitates reduction in dosage. Diurnal variations in blood pressure require administration of lower doses in the morning than those given in the afternoon and evening. Seasonal variations also alter the hypotensive effect of mecamylamine, larger doses being required in the winter months than in the summer. It should also be remembered that ordinarily a smaller reduction in blood pressure is produced by the drug when the patient is in a supine or sitting position; therefore, dosage should be determined on the basis of blood pressure readings made with the patient in the standing position. Since frequent standing blood pressure recordings under basal conditions afford the best method for accurate dosage adjustment, these are best carried out in the home by the patient or a member of the family.

Therapy is initiated by the administration of 2.5 mg. twice daily. This dosage is then increased by increments of 2.5 mg. at intervals of not less than two days until the desired blood pressure response has been obtained. The average daily dose required for maintenance is about 25 mg. in three divided doses. Individual susceptibility to the drug is so great that as little as 1 mg. may mean the difference between tolerable and intolerable side-effects.

Applicable commercial name: Inversine Hydrochloride.

Merck Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of mecamylamine hydrochloride.

COUNCIL ON MEDICAL PHYSICS

Report of the Council

The Council has authorized publication of the following report.

Ralph E. DeForest, M.D., *Secretary.*

PROGRAM OF THE COUNCIL ON MEDICAL PHYSICS

The Council on Medical Physics, a standing committee of the Board of Trustees of the American Medical Association, is composed of 13 members from various fields of medicine and the basic sciences. The members were chosen because of the special knowledge that they have, and not as representatives of specialties. The Council was created by the Board of Trustees in accordance with the actions of the House of Delegates at the Clinical Meeting in Boston, Nov. 29-Dec. 2, 1955,[1] and at the Annual Meeting in Chicago, June 11-15, 1956.[2]

The purpose of the Council on Medical Physics is to encourage an understanding of the actions and rational uses of apparatus and physical methods employed in the study of the human body and its functions, notably the diagnosis, treatment, and prevention of disease. Since the physical methods used in medicine are explained in terms of the sciences of physics, biophysics, and medicine, the Council was named Council on Medical Physics. In pursuit of this purpose, the Council program will consist of the evaluation of classes of apparatus and physical methods, the encouragement of research, and the performance of such other services within its purview that may be assigned by the Board of Trustees or decided upon by the Council.

Apparatus and Physical Methods Evaluation.—The Council evaluates, when desirable, new, previously considered, or established classes of physical methods and apparatus intended for the diagnosis, treatment, and prevention of disease. The evaluation statements contain, where applicable, the principles, actions, uses, contraindications, and appropriate safety warnings regarding the use of the class of apparatus or physical method being reported upon. These reports are submitted to the Editor of The Journal for publication in the Council column.

The Council's evaluation statements are prepared after consideration of scientific clinical and laboratory evidence concerning a class of apparatus or a method and after consideration of other available evidence, including published and unpublished reports. The Council obtains opinions from experts in the field who serve as consultants. The Council itself does not conduct clinical or laboratory tests, experiments, or research in evaluating apparatus or physical methods.

It is important to note that the Council does not consider individual brands of apparatus but reports only on general classes of apparatus. Occasionally, a device made by only one manufacturer may constitute a new idea or method of treatment. In this instance, although the device name and model will not be mentioned, the general principles employed in any such class of apparatus will be discussed. No endorsement or guarantee of any specific brands of apparatus is intended or implied.

The Council decides whether to undertake the evaluation of the evidence pertaining to a class of medical apparatus or physical method. Manufacturers are encouraged to cooperate with the Council by providing data and information, including scientific laboratory and clinical evidence (published and unpublished reports), regarding the usefulness, safety, actions, mode of operation of, and contraindications for their apparatus, if it falls within a class the Council has voted to evaluate. Before compiling and providing any such data and information for the Council, the manufacturer should contact the Secretary of the Council on Medical Physics, American Medical Association, 535 N. Dearborn St., Chicago 10, Ill., to determine whether the Council is considering, or will consider, the evaluation of the evidence relating to that particular class of product.

All available evidence, including the opinions of the Council consultants on such evidence, is submitted to a Council referee. The referee makes his recommendations regarding the evaluation report, which may be prepared either by the Council staff or by an author designated by the Council. This report, together with the referee's recommendation, consultants' comments, and copies of the available evidence, is provided to all the Council members for consideration. The proposed evaluation report is then reviewed and revised in accordance with the comments of the members. After adoption by vote of the Council, a copy of the report will be sent for comment to known manufacturers. Comments and criticisms received from the manufacturers are considered before the report is sent to the Editor of The Journal for publication.

As another activity, the Council will compile informative articles on the role of physical agents and methods in the care of patients with specific diseases, as well as such articles in general and special areas of medical practice.

Encouragement of Research.—The Council desires to encourage needed research on practical problems involving apparatus and methods falling within the scope of medical physics. The Council does not finance research or conduct clinical and laboratory projects itself. The Council plans to point out areas in which research is needed and will attempt to facilitate the development of sound investigative programs leading to the production of scientific evidence necessary in evaluating the usefulness of clinical devices, apparatus, and instruments. The value of such evidence is apparent to the manufacturer and the profession.

Progress by the medical profession in the application to medicine of new contributions from all branches of physics and engineering is proceeding at an ever-increasing rate. New devices and the new methods they employ are in many instances unfamiliar to most practitioners. An appreciation of the actions and rational uses of these apparatus and methods is desirable if the best interest of the patient is to be served. The Council intends, through its program, to provide a useful and valuable information service to the profession.

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Shields Warren, M.D.
George F. Lull, M.D. (ex officio)
Ernest B. Howard, M.D. (ex officio)
Austin Smith, M.D. (ex officio)

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2. Report of the Board of Trustees, Council on Medical Physics, J. A. M. A. **161:** 157 (May 12) 1956. Proceedings of the House of Delegates of the American Medical Association, Annual Meeting, Chicago, June 11-15, 1956, J. A. M. A. **162:** 482 (Sept. 29) 1956.

MEDICINE AT WORK

DOCTOR, TAKE THE STAND

Almost unnoticed, two great professions—medicine and law—are teaming up in a new public service effort that promises to save the taxpayers millions of dollars a year.

Director C. Joseph Stetler of the American Medical Association's Law Department was concentrating not on taxes but on a legal point nearly two years ago during his summer vacation. His point was that, with medical testimony figuring as key evidence in about three out of every four court actions, the doctor and the lawyer should get to know one another's work a little better. His point was that many doctors were not doing their best on the witness stand, often because just as many lawyers were not doing their best in bringing out enough clear medical evidence. Stetler's point was that this lack of rapport was impeding the administration of justice.

Invariably in situations of this sort, the suffering is felt most deeply not by the physician or attorney but by the general public—ranging from the plaintiff or defendant whose case is not presented fairly to the unrelated man on the street who must foot most of the bill for the trial.

So Stetler carried on a policy begun back in 1914 when the A. M. A. House of Delegates voted acceptance of a three-year survey report pointing up the important role of the physician as a medical witness. (That policy also set the stage for closer doctor-lawyer cooperation outside the courtroom, such as the creation of a joint committee on narcotics addiction and joint conferences on chemical tests for motorist intoxication.)

Stetler wrote a skit illustrating the boners pulled by both physicians and attorneys in a hypothetical court case. Here, the doctor is useless to a railroad man trying to collect damages for a permanent back injury. The physician shows himself as a bungling amateur. He is unprepared with records, slipshod in memory, and so verbose in terms not understood by the jury that he sounds like an ancient medical textbook. This spectacle, coupled with a skillful defense presentation, is all the "reasonable doubt" that the suspicious jury needs to decide against awarding damages for the injured man.

Proper Presentation

In the second half of this before-and-after story, both the physician and the injured man's lawyer are so well-prepared (with the doctor using a shadow box to illuminate x-rays and the attorney expressing his familiarity with medical examination methods) that the jury easily understands what is being presented.

That skit had its première before an audience of 300 at a medicolegal symposium in Chicago Oct. 9, 1955. Aside from making medical matters clearer to attorneys, and vice versa, the session accomplished something equally important. It had doctors and lawyers regarding each other with new respect. The symposium idea began spreading across the country, often bringing together both professions for the first time in their community's history. Such was the case in Peoria, Ill., recently, where 300 physicians and attorneys assembled in a somewhat cagey atmosphere.

Then they viewed the play, viewed each other's viewpoints of the performance, and very much liked what they saw. It was a heartening occasion.

The one-hour play has been enacted successfully for the two professions at meetings in a dozen cities—including New York, Omaha, Denver, Fort Wayne, Ind., Atlanta, Ga., and Des Moines, Iowa. There were three presentations before state medical association houses of delegates and one for a comparable bar association body. At least three more performances are scheduled in coming weeks. Several local groups, impressed with the response at regional meetings, have written similar scripts of their own.

By late fall, Stetler decided that the demand called for reaching a relatively mass market in medicine and law. So the A. M. A. and the American Bar Association, in cooperation with a Cincinnati pharmaceutical house, the Wm. S. Merrell Company, produced a 35-minute film version of the play in the New York City studios of Dynamic Films, Inc. Shooting on the script took one week, and "The Medical Witness" was premièred last Nov. 27 at the A. M. A. Clinical Session in Seattle for hundreds of physicians and attorneys. There was such interest in the film that two showings were needed to accommodate standing-room audiences.

This week the motion picture is being made available without charge, through the A. M. A. film library, to law and medical societies and schools across the nation. It is the first in a series of six movies on medicine and the law.

Really, it is for the interest of all. For example, in New York City each day of a trial costs the taxpayers at least $750. The average trial lasts about three days, for a total of $2,250. So it is readily apparent that expert medical testimony in its fairest sense—when applied to the heavily congested court calls of New York, Chicago, Detroit, Philadelphia, Los Angeles, and many other cities—not only would reduce the number of trial days but also would result in the settlement of cases prior to the trial stage.

Large Dollar Sign

What attorney would risk the possibility of losing a questionably proved case when he is reasonably certain of an effective medicolegal counterattack? Expand that picture to cover the multitude of cases on file throughout the land and the view is bound to focus on a large dollar sign: millions of dollars saved annually.

Certainly, the gains to justice through closer liaison between doctors and lawyers are more than monetary. Another benefit lies in greater public respect for both professions, resulting in increased confidence generally in the administration of justice and in medical practice. This, in turn, would tend to encourage expert testimony from many physicians who in the past have recoiled in disgust at two sights: the ignorant and corrupt medical man who hires himself out as a partisan for one side or the other, and the lawyer who fosters it by calling for a wrongful slant on medical testimony.

As A. M. A. President Dwight H. Murray put it last August at an American Bar Association meeting in Dallas: "I am convinced that the major portion of the difficulty with medical expert testimony stems from the minority of cases wherein the system is not so much at fault as are the men—of your profession and mine—who pervert the system to their selfish ends."

Both the A. M. A. and the A. B. A. believe that medicolegal skulduggery in the courts is the exception rather than the rule. More common is the case in which a perfectly honest and sincere doctor and lawyer unintentionally bring about a miscarriage of justice through improper or confused presentation of the facts. When evidence is presented thoroughly and accurately so that a just decision can be made, the doctor-witness and the lawyers for both sides find themselves speaking the same language.

Who can say what unforeseen additional benefits may accrue from this growing tendency of physicians and lawyers to join in the quest for justice—not through being forced together by legislation, but by the more solidifying experience of voluntary cooperation? The doctor, more than any other professional man, is called as a key witness in court actions. Perhaps his greater accord with men of law will set a clear pattern for experts in other arts and sciences who often are handicapped within their own specialties when they are called upon for evidence.

Meanwhile, uppermost now in this new and sweeping doctor-lawyer rapport is the promise of less abuse and deficiency in the field of expert medical testimony. It can mean less delay from the fantastic pileup of pending damage suits, increased knowledge of their own and one another's range of endeavor, and the prospect of future accord in all matters of mutual interest for the welfare of their fellow man.

Left, in this scene from the motion picture "The Medical Witness," the physician on the stand tries to illustrate his testimony with an x-ray film that would be unclear to the jurors even if the lawyer were not blocking their view.

Center, a shadow box is used to illuminate a diagnostic finding from the same x-ray picture—so that the jury can see the basis of the expert medical testimony in the same case.

Right, Dr. David B. Allman, A. M. A. President-Elect (left), joins with president David F. Maxwell of the American Bar Association in presenting the new medicolegal film "The Medical Witness" at the A. M. A. Clinical Session in Seattle.

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION
Edited Under the Direction of the Board of Trustees

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Subscription price . . Fifteen dollars per annum in advance
Cable Address . . . . "Medic, Chicago"

BLOOD GROUP PARADOXES

GUEST EDITORIAL

Alexander S. Wiener, M.D.
and
Irving B. Wexler, M.D.

Up to a decade ago, descriptions of clinical investigations frequently suffered from a failure to apply statistical methods. Investigators have since become so sensitized to the value of biometrics that nowadays rarely does an article appear without its standard errors and chi squares duly recorded. Unfortunately, at the same time there has been a tendency to overlook the fact that mathematics is no substitute for common sense. If the premise from which an investigation starts is false and the observations inaccurate, even the most painstaking calculations will lead to erroneous conclusions. A possible example of this is provided by the recent epidemic of articles dealing with the distribution of the blood groups in various diseases.

More than 20 years ago studies on the distribution of the ABO blood groups in disease enjoyed considerable vogue. At that time, the blood groups were studied in such conditions as dementia precox, malaria, general paresis, migraine, epilepsy, longevity, various skin diseases, bone and joint tuberculosis, dental caries, susceptibility to poliomyelitis, and many other conditions. However, whenever a supposed cor-

the disease and predominately brown-eyed, it would be found that in a random sampling of the entire population relatively more people with brown eyes would have the disease. This explanation rarely had to be invoked, however, since in most of the cases the real difficulty proved to be faulty methods of collecting the data. Eventually, workers in the field realized the inherent fallacies in these studies, and it was accepted that the ABO groups had no effect on health, except in hemolytic disease of the newborn infant, where isosensitization of the mother provided a logical explanation. Recently, however, investigations of this type have been resumed on a large scale.

During the past few years, reports have been published purporting to show an association between blood groups and such conditions as duodenal ulcer, gastric carcinoma, pulmonary cancer, rheumatic fever, sarcoidosis, diabetes mellitus, pernicious anemia, fertility, pituitary adenomas, fractured femurs, Dupuytren's contracture, bronchiectasis, portal cirrhosis, bronchopneumonia in childhood, arteriosclerosis, and hypertension. In some cases the technique of blood typing is suspect, as in the report that claimed that every one of 28 patients with Dupuytren's contracture belonged to type Rh_1Rh_2. In one of the newer studies reporting an association between duodenal ulcer and group O, a study that is made impressive by virtue of the large size of the series involved, the controls consisted of tens of thousands of blood donors typed within a short period of time in a blood donor center, while the experimental group was culled from the records of many hospitals over a period of several years. This difference in the method of compiling the data in the two series may have introduced a bias into the results. Significantly, when instead of using random donors as controls the relatives of affected individuals were used to make up the control series, the supposed correlation between blood group O and duodenal ulcer could not be confirmed.

Also of interest is a recent report claiming a supposed association between carcinoma of the body of the stomach and blood group O. In the control series of 30,000 blood donors, 48.9% proved to be of blood group O, while, among 225 patients with carcinoma of the body of the stomach, as many as 68.4% belonged to group O. These 225 were part of a larger series of 483 individuals, all of whom had carcinoma of the stomach, the difference being made up of two groups no great significance is ordinarily attached to differences far greater than have been observed in most of the studies on blood groups in disease.

One wonders how many readers who may have been impressed by the reported association between blood group A and fractured femur have pondered the possible pathway through which one's blood group could influence the occurrence of a fracture. Before too much energy is expended on such an exercise, let the thoughtful clinician remember that the hardest things to explain are those that are not true.

THE GENERAL PRACTITIONER'S AWARD

In accordance with the now well-established practice, the House of Delegates of the American Medical Association, on November 27, at the 10th Clinical Meeting in Seattle, named Dr. Edward M. Gans of Harlowton, Mont., the General Practitioner of the Year. The gold medal, designed especially to go with the award and to honor a general practitioner who has rendered exceptional service to his community, has been given annually since 1948. Dr. Gans, who has practiced medicine for 51 years, has practiced for 44 years in the Harlowton area. He was born December 27, 1875, at St. Cloud, Minn., and was graduated from the University of Minnesota Medical School in 1905. After an internship spent in the city of Duluth, Dr. Gans moved to Eveleth in Minnesota's famous iron mountain country, where he practiced for six years, then moved on to Dickinson, N. D., for one year, and in 1912 moved on to Judith Gap near Harlowton.

Edward M. Gans, M.D.

Always interested in community affairs, Dr. Gans was first health officer and then was elected mayor of Judith Gap, which position he left in 1917 to serve as a captain in the United States Army Medical Corps in France during World War I. After the war he returned to practice medicine in Judith Gap until 1929 and then moved to Harlowton. Dr. Gans was president of the Montana Medical Association in 1930, and in 1955 he became eligible and was made a member of that association's Fifty Year Club. He is one of the few physicians who has been in active practice in Montana for 50 years. Now 81 years of age, he is still active in the practice of medicine.

Dr. Gans has two sons following in his footsteps. The older, Dr. Paul Gans, is practicing in Lewistown, Mont., and the younger, Dr. Edward Gans, is practicing otolaryngology in Oakland, Calif.

The nine physicians who have received the General Practitioner award since the first was chosen in 1948 are Archer Chester Sudan, Kremmling, Colo.; the late William L. Pressly, Due West, S. C.; Andy Hall, Mount Vernon, Ill.; the late Dean Sherwood Luce, Canton, Mass.; Albert C. Yoder, Goshen, Ind.; John M. Travis, Jacksonville, Texas; the late Joseph I. Greenwell, New Haven, Ky.; Karl B. Pace, Greenville, N. C.; and E. Roger Samuel, Mount Carmel, Pa.

ANNUAL CONGRESS ON INDUSTRIAL HEALTH

The year 1957 will mark a milestone in the history of the Council on Industrial Health, which will have completed 20 years of work in striving to make occupational health programs serve more effectively in complementing the services of clinical medicine and community health. Its program has evolved over the past 20 years from one of limited interests to one in which it has assumed leadership in a number of fields, particularly in the improvement of communication and cooperation between management, labor, the medical professions, and other groups concerned with employee health. One of the activities of the Council on Industrial Health is the Annual Congress on Industrial Health, which has become a nationally recognized medical forum. The wide range of discussions in previous annual meetings reflect both its interests and the current issues and problems that are of present-day concern to all those involved in maintaining high standards of occupational health.

The 17th Annual Congress on Industrial Health, to be held in Los Angeles, February 4-6, 1957, with its theme of "Spotlight on Burns-Vision-Pesticides-Noise" reveals one aspect of the Council's work. The technical discussions to be presented in connection with such topics as Vision in Industry, Health Hazards of Agricultural Chemicals, New Concepts in the Management of Burns, and New Developments in Hearing Loss due to Industrial Noise are demonstrations of the type of program and information the Council seeks to disseminate to the widest extent possible. The sessions planned will present new and hitherto unpublished data surrounding various developments in these fields of inquiry. The congress participants are acknowledged leaders in their fields, and their contributions will stimulate discussion and further inquiry for the medical and allied professions.

The detailed program of the forthcoming Annual Congress on Industrial Health (this issue, page 1478) speaks well for a highly rewarding meeting. The program spotlights more than a group of important discussions; it focuses attention on the kind of activity the American Medical Association encourages and stimulates in its quest to protect the health of the American worker.

ORGANIZATION SECTION

ADDRESS OF THE PRESIDENT

Dwight H. Murray, M.D.

Almost six months have elapsed since we last met to deliberate and act on medical affairs. The time has passed quickly, but not quietly. The rumble of war and revolution has resounded in our ears. The din from political battles has been deafening.

All of us—sooner or later—learn that today's events do not just swirl around us, but involve each of us. As doctors we cannot get away from them by claiming that our only interest is in the sick and that we cannot be bothered by political, social, and economic problems. These matters demand attention from the doctor as well as the lawyer, the businessman, the newspaper editor, the labor leader, and the worker.

If we are concerned about what happens on the international, national, and local fronts—and we should be—then certainly we cannot afford to be disinterested in what happens in our own area of health and medical affairs. Yet there is apathy in our ranks.

Replace Apathy with Active, United Profession

Today there is a greater need for a united, forceful, and informed profession than ever before. We have been caught in the throes of a social revolution which demanded something for nothing. Changes have been taking place all around us, and medicine has not escaped unscathed. For example, in a few days Public Law 569, the bill providing medical care for military dependents, becomes effective throughout the land. Contracts already have been signed with the government by the majority of our state societies. No longer can any doctor claim that this law does not affect him. No longer can he say that government laws really are not changing the practice of medicine.

Public Law 880, better known to all of us as H.R. 7225, is another case in point. Medicine now is facing the problem of protecting the taxpaying public from abuses and of cooperating with the government to carry out the provisions of the law. The law is now on the books, and we must provide the leadership necessary to make it work as well as possible.

It was encouraging to hear Ezra Taft Benson, Secretary of Agriculture, say last week before the American Association of Land Grant Colleges and Universities:

> Sooner or later, the accumulation of power in a central government leads to a loss of freedom. . . . Raids on the federal treasury can be all too readily accomplished by an organized few over the feeble protests of an apathetic majority. With more and more activity centered in the federal government, the relationship between the cost and the benefits of government programs becomes obscure. What follows is the voting of public money without having to accept direct local responsibility for higher taxes. . . . If the present shift of power from state to federal authority which started 25 years ago is allowed to continue, the states may be left hollow shells.

It was encouraging to hear such comments from a member of the President's Cabinet. I only wish that all members of the official family and, more important every member of the United States Congress felt the same way.

The expression of this philosophy, with which medicine so heartily agrees, sounds good, but putting it into practice is the thing we are really interested in.

Today the medical profession along with business and industry is caught between those who desire to promote sound government and those who desire even more intensely to perpetuate party power. Unfortunately, in recent years a benevolent federal government appears more attractive to the voting public than the preservation of individual freedom. Medicine must do its utmost to reverse this trend.

Medical Freedom Essential

In my travels around the country as your representative the last 18 months, I have seen little dissension or rancor within our ranks. However, I must report that I have seen too much complacency over governmental encroachment into medical affairs. And I am deadly serious when I say to you that apathy by the few, or by the many, can be detrimental to all.

No nation can merely reap the benefits of freedom; it also must sow seeds of freedom. In medicine the situation is the same. If an apathetic medical profession takes its freedom for granted, it will be the beginning of the end. A strong, free profession must work for freedom so that it may live in freedom. And history tells us that once medicine loses its freedom, other fields of private endeavor are immediately in danger.

I do not wish to paint a dark or distorted picture of medicine's free status and its stature in America today. But I do believe words of caution and an appeal for vigilance are in order. The road of apathy and disunity can lead only to disorder and perhaps disintegration, and we must sound a warning to all our colleagues who do not care, or who are pulling in the opposite direction. The road of alertness, action, and unity is the proper road for all of us to be traveling together.

If I had just one wish for the coming year, it would be to command the time and talents of the 160,000 physicians in the American Medical Association. I would set us all to the task of emphasizing and re-emphasizing the absolute necessity of patient and professional freedom.

Patient's Right to Choose His Doctor

I believe it is one of our prime responsibilities to prove to our patients that their right to choose their doctor is a most important one. Free choice brings a bond of confidence between doctor and patient which no compulsory medical system can create. It means that the patient knows the physician will be interested in him as a person, not as just a serial number of the 2:45 appendicitis case.

Read before the House of Delegates at the 10th Clinical Meeting of the American Medical Association, Seattle, Nov. 27, 1956.

For the doctor free choice means that the patient has selected him for his abilities, training, sincerity, and personality. When a patient comes into my office, I know he has made a choice. And from that moment there begins a physician-patient relationship of the highest order. To me the patient is someone special, and I in turn hope I am someone special to him.

Once the patient has made his choice, the physician automatically assumes an unqualified responsibility to the patient. No system of medical care that uses a third party to bring doctor and patient together can match our kind of cooperative performance for the treatment of illness, the cure of disease, and the betterment of the patient's health.

Freedom to select a doctor is part of everyone's great freedom to choose—to choose what he wears and eats, where he works and worships, and how he votes. Take away any part of this freedom and great damage is done to our democratic system.

Free Conduct in Medical Treatment

Another freedom closely tied to freedom of choice is freedom in the conduct of medical treatment. At the recent meeting of the World Medical Association in Havana, Cuba, Dr. Rolf Schloegell of Germany made a stirring defense of free conduct of medical treatment. He told us that the medical profession believes the attending physician alone is competent to decide what measures he deems necessary and will apply in order to bring about the desired improvement. He warned too of the danger of excessive restriction on the freedom of the patient and the attending doctor.

Yet the trend toward extending social security in the medical care field has been steady and has accelerated since the end of World War II. The dangers of shifting responsibilities for medical care from the patient and doctor to the government are obvious. The caliber of medical care cannot be as high when both patient and doctor are dependent upon government. Initiative succumbs to dictation, and self-reliance is replaced by the crutch of government.

We do not deny that there is an area of legitimate concern by the government for the health and welfare of the people. But each year government seems to extend that area. We get some idea of this expansion from the new federal medical budget. This year, according to our Washington Office, the average family will be paying $54.61 for the U. S. government's health and medical activities. And the total expenditures this year amount to 2.5 billion dollars—290 millions more than last year. Even in an over-all federal budget of 61 billion dollars, the total health cost of 2.5 billions is not insignificant. It is a billion dollars more than the cost of running the Commerce Department, half a billion more than that of running the Agriculture Department, and six times more than the Interior Department's budget.

Many expenditures obviously are necessary to keep up our unsurpassed public health standards, and research may pay rich dividends in scientific discoveries. But there is no doubt that much money is being spent on medical activities that should not involve government participation.

The trend is to spend more and more government money on health and medical matters because it is good politics. Apparently many Americans still want to see government in the role of a big brother, dishing out so-called gifts and bargains under the guise of benevolent economic planning.

I believe it is our duty, as it is everyone else's, to combat the attitude of "what's in it for me?" and to promote the long-honored creed of "what's best for all Americans and our free society?" I think that a nation can drift into state medicine inch by inch just as surely as if the scheme were foisted upon a people overnight. The "drift" method may take longer, but the result will be the same.

So it is time all of us sounded the alarm against soft and superficial security and against the invasion of personal responsibility. It is time we stood up together for militant freedom and for full rights and responsibilities of the individual.

Belgian Doctors Turn Back Government

There is no better example of what a unified medical profession can do than in the story of the recent fight of the Belgian doctors against the government's proposals for a state service of medicine.

Without consulting the medical profession the Belgian government proceeded to draft rules and regulations of health to be incorporated in the nation's social security legislation. Under the proposals doctors were to sign an agreement to abide by the present rules and any later regulations. For the patient there would be the usual red tape in getting medical care.

When the Belgian doctors learned of the scheme, they met in conference with the government. They told the government what they wanted and what they would not accept. The government agreed. For several months everything was quiet. Then the Belgian doctors suddenly read about the new health bill that the government was sending to Parliament. It was quite contrary to the earlier agreement worked out by the profession and the government. But the bill was passed quickly.

The Belgian medical profession protested and said it would not be placed under the Ministry of Labor. Instead the doctors proposed to set up their own plan of medical assistance. Before long, the government saw that the medical profession meant business and that the doctors' plan was an attractive one. So it declared that its own bill was not in force and could not be in force without the consent of the medical profession.

To me this fight against legislative intervention in medical care is excellent evidence that the profession can defend itself if it unites to defend the basic principles of freedom and if it offers constructive proposals. By using the Belgian national motto, "in union there is strength," the medical profession showed doctors everywhere that dangerous government plans can be turned aside by the strong.

I also read recently in the journal of the World Medical Association of the fight of the medical profession of Malta against a British government scheme to introduce a full-time salaried medical service, without the right of private practice, on an island dependency of Malta. Here again the doctors reacted with unity and strength, and successfully thwarted the government's plan.

There is a lesson in these stories from Belgium and Malta. They prove that a unified profession has a great political power for good—the good of the patient, the doctors, and the nation.

Confidence of Patients, Understanding of Legislators Needed

While we are developing unity within our own ranks, I believe it is equally important to continue to build up the confidence and respect of our patients, and to make our legislators aware of the necessity for freedom in medical practice.

Let us never reduce the quality of service we render to our patients, and never lose the personal touch in medicine. Where there is any opportunity to improve upon our medical care, let us seize it and show our abilities to do an outstanding job. Satisfied patient-customers will give us deserving support when we need it.

We also should realize that the destiny of medicine can be determined to a large degree in the halls of Congress. If this be true, then it is even more important that we take an even greater interest in those who elect the congressmen. Sympathetic understanding of our position by federal legislators through the voting public will be an insurmountable deterrent to the forces supporting state medicine.

The day has come, gentlemen, when we can no longer look upon medical economics and social changes merely as issues to be considered during our limited leisure hours. Our interest in them cannot be superficial or intermittent. We now must pay daily attention to these matters. Medical socioeconomic affairs can no longer be just incidental with us. They must be a vital part of our life and of our profession.

Each of us, I believe, should dedicate himself to the words included in the oath of office taken by the President of the A. M. A.: "I shall champion the cause of freedom in medical practice and freedom for all my fellow Americans."

As doctors, representatives to the A. M. A., and spokesmen for the A. M. A., let us remember these words and live by them. And to alter a phrase of President Lincoln's only slightly: Let's make common cause to keep the good ship of medical freedom on this voyage, or nobody will have a chance to pilot her on another voyage.

ANNUAL CONGRESS ON INDUSTRIAL HEALTH

"SPOTLIGHT ON VISION-PESTICIDES-NOISE-BURNS"

Co-sponsors:
California Medical Association
Los Angeles County Medical Association
Northwest Association of Occupational Medicine
Western Industrial Medical Association

The Council on Industrial Health of the American Medical Association announces the following details regarding the 17th Annual Congress on Industrial Health, to be held at the Biltmore Hotel in Los Angeles, Feb. 4, 5, and 6, 1957. The technical discussions and scientific exhibits are open to all physicians, nurses, industrial hygienists, engineers, and others interested in occupational health. There is no registration fee.

VISION IN INDUSTRY

A Comprehensive Examination of Fundamentals and Fine Points

PRESENTED IN COOPERATION WITH THE NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

PART I

Monday, Feb. 4, 2 p. m.
Chairman—FRANKLIN M. FOOTE, M.D., New York
Components of a Complete Vision Program
FRANKLIN M. FOOTE, M.D., New York
A Critical Evaluation of Vision Screening Methods
MICHAEL J. HOGAN, M.D., San Francisco
Testing for Color Perception
DEAN FARNSWORTH, New London, Conn.
Estimation of Loss of Visual Efficiency
EDMUND B. SPAETH, M.D., Philadelphia
Relationships Between Illumination and Vision
H. RICHARD BLACKWELL, Ph.D., Ann Arbor, Mich.

PART II

Tuesday, Feb. 5, 9 a. m.
Chairman—EDMUND B. SPAETH, M.D., Philadelphia
Responsibilities and Limitations of the Industrial Nurse in the Vision Program
MARGARET HARGREAVES, R.N., New York
Elements of a Successful Eye Protection Program
JAMES E. O'NEIL, New York
RICHARD WILKINS, Los Angeles
The Prescription Safety Goggle Problem
E. J. SCHOWALTER, M.D., Chicago
Emergency Treatment of Chemical Injuries to the Eye
RALPH RYAN, M.D., Morgantown, W. Va.
Screening for Eye Disease
FRANKLIN M. FOOTE, M.D., New York

HEALTH HAZARDS OF AGRICULTURAL CHEMICALS

Tuesday, Feb. 5, 2 p. m.
Co-Chairmen—LEMUEL C. MCGEE, M.D., Wilmington, Del.
RUTHERFORD T. JOHNSTONE, M.D., Los Angeles
Agricultural Chemicals—Economic Facts, Laws and Regulations
ALLEN LEMON, M.D., Sacramento, Calif.
The Phosphorous-Containing Insecticides—Toxicology, Clinical Symptoms and Treatment
H. H. GOLZ, M.D., New York
The Chlorinated Organic Insecticides—Toxicology, Clinical Symptoms and Treatment
FRANK A. PRINCI, M.D., Cincinnati
Control of Hazards in the Use of Agricultural Chemicals—California Experience
ROBERT L. METCALF, M.D., Riverside, Calif.

BANQUET

(Informal)

Tuesday, Feb. 5, 7 p. m.
Presiding—WILLIAM P. SHEPARD, M.D., New York
Presentation of Award of the President's Committee on Employment of the Physically Handicapped
Address
DWIGHT H. MURRAY, M.D.
President, American Medical Association
Address
ERNEST B. HOWARD, M.D.
Assistant Secretary, American Medical Association

NEW CONCEPTS IN THE MANAGEMENT OF BURNS

Wednesday, Feb. 6, 9 a. m.
Chairman—PAUL S. RICHARDS, M.D., Salt Lake City
Brief Historical Résumé of the Subject
PAUL S. RICHARDS, M.D., Salt Lake City
Dry Aluminum Powder Therapy for Thermal Burns
M. D. MAXMEN, M.D., Toronto, Canada
The Exposure Method of Treatment
GEORGE T. VAN PETTEN, commander
Medical Corps, U. S. Navy, Newport, R. I.

Research in the Treatment of Burns
Robert D. Pillsbury, Lieut. Col., Medical Corps, Surgical Research Unit, Brooke Army Medical Center, Fort Sam Houston, Texas
Oral Treatment of Burn Shock
Kehl Markley, M.D., Philadelphia

NEW DEVELOPMENTS IN HEARING LOSS DUE TO INDUSTRIAL NOISE

Presented in cooperation with the
Subcommittee on Noise in Industry,
Committee on Conservation of Hearing,
American Academy of Ophthalmology and
Otolaryngology

Wednesday, Feb. 6, 2 p. m.
Chairman—James H. Sterner, M.D., Rochester, N. Y.
Methods for Conservation of Hearing
Howard P. House, M.D., Los Angeles
Status of Research Activities of the Subcommittee on Noise in Industry
Aram Glorig, M.D., Los Angeles
What Constitutes Disability and How Is It Measured
Hallowell Davis, M.D., St. Louis
Allowable Noise Exposure for Hearing Conservation
Walter A. Rosenblith, Boston
Teamwork Solution of the Industrial Noise Problem—Successful Coordination of the Activities of the Medical Director, the Consulting Otologist, the Industrial Hygienist, the Audiometric Technician, the Safety Engineer, the Supervisory Staff, the Plant Engineer, the Personnel Director, and others
Paul J. Whitaker, M.D., Milwaukee

The Scientific Exhibits will include a number directly related to the technical discussions:

Treatment of Burns
Burn Management in the USS Bennington Disaster
Phosphate Ester Insecticides
Pesticides
Accidental Poisoning in Children
Testing for Eye Disease
Demonstrations of Vision Testing Devices
Speech Audiometry
Automatic Audiometry
Multiple Audiometry
Research in Noise

Special tours of the research laboratories of the Subcommittee on Noise in Industry are scheduled for Monday, Feb. 4, at 10 a. m. and 8 p.m., and Thursday, Feb. 7, at 10 a. m. Advance reservations are desirable due to limitations on the size of the group that can be accommodated.

A hospitality committee will assist sightseeing visitors in planning trips to points of interest such as Disneyland, Farmers' Market, Old Mexico in Olvera Street, the Old Spanish Missions, Catalina, Knott's Berry Farm and Ghost Town, the Huntington Library and Art Galley, and famous restaurants. Regular tour service will also be available.

WORLD MEDICAL ASSOCIATION ELECTS OFFICERS

At its 10th General Assembly held in Havana, Cuba, Oct. 9-15, 1956, the World Medical Association elected the following officers:

President—1956-1957
Dr. Jose A. Bustamente, Cuba
President-Elect—1956-1957
Dr. Ahmet Rasim Onat, Turkey
Treasurer—1956-1959
Dr. Ernst Fromm, Germany
Members of Council—1956-1959
Dr. Gunnar Gundersen, U. S. A.
Dr. Marcel Poumailloux, France
Dr. S. C. Sen, India
Dr. Lorenzo Garcia-Tornel, Spain

The Council of The World Medical Association elected the following officers for the coming year:

Chairman of Council
Dr. Lorenzo Garcia-Tornel, Spain
Vice-Chairman of Council
Dr. L. R. Mallen, Australia

The Officers of Committees for 1956-1957 include:

Editorial Board
Dr. Austin Smith (U. S. A.), Chairman
International Liaison
Dr. Jean Maystre (Switzerland), Chairman
Medical Education
Sir Lionel Whitby (U. K.), Chairman
Medical Ethics
Dr. P. Glorieux (Belgium), Chairman
Miscellaneous Business
Dr. Otto Rasmussen (Denmark), Chairman
Planning and Finance
Dr. T. C. Routley (Canada), Chairman
Social Security
Dr. Dag Knutson (Sweden), Chairman
Dr. Rolf Schloegell (Germany), Secretary

The Council appointed the following officers:

Regional Secretaries
Asia—Dr. S. C. Sen, India
Australasia—Dr. John Hunter, Australia
Europe—Dr. Paul Cibrie, France
Latin America—Dr. Hector Rodriguez H., Chile
World Medical Journal Officials
Dr. Austin Smith (U. S. A.), Executive Editor
Dr. Stanley S. B. Gilder (Canada), Associate Editor
Dr. Louis H. Bauer (U. S. A.), Business Manager
Liaison Officers
Dr. Jean Maystre, Switzerland
Dr. P. Glorieux, Belgium
Dr. V. A. Fenger, Denmark

The New Zealand Branch of the British Medical Association was elected to membership in the World Medical Association at the 10th General Assembly. This association was organized in 1896 and has approximately 810 members.

The following are among numerous resolutions adopted by the 10th General Assembly of the World Medical Association:

International Medical Law

"It is the primary function of the medical doctors of the world to formulate any code of International Medical Law and The World Medical Association is the only organization that can speak for the doctors of the world."

Traffic Accidents

"Whereas: The death and maiming of humanity throughout the world is increasing rapidly each year; and

"Whereas: It is the duty and responsibility of the medical profession in every country of the world to assist in the preservation and maintenance of human life;

"Therefore, be it resolved: That The World Medical Association recommend to its member associations that they cooperate with other agencies and authorities within their country to whatever degree is possible and necessary in a concentrated endeavor to save and preserve human life."

MEDICAL NEWS

ALABAMA

Public Health Physicians Needed.—According to the *Journal of the Medical Association of the State of Alabama*, a critical shortage of public health physicians exists in that state. Health officers are employed under three classifications, according to standards set by the state merit system: health officer 1, $500-$700 a month; health officer 2, $600-$800 a month; and health officer 3, $700-$900 a month. The applicant should be under 60 years of age, in good health, licensed or eligible for licensure to practice in Alabama, and a member or eligible for membership in a county medical society. Information may be obtained from the State Health Officer, 501 Dexter Ave., Montgomery 4.

Evacuation Hospital in Training.—The 109th Evacuation Hospital of Birmingham, Alabama National Guard, has returned from two weeks of training at Fort McClellan near Anniston. Under the command of Col. Samuel R. Terhune, the hospital gave medical support to the nondivisional units of the Alabama National Guard in training at Fort McClellan and concurrently conducted sectional training. The following section chiefs assisted: Lieut. Col. Jo R. Hood, Birmingham, chief of surgery; Lieut. Col. James G. Wood Jr., chief of x-ray; Lieut. Col. Howard F. Pringle Jr., D.D.S., Mobile, chief of dental section; Major John T. Strickland, Birmingham, chief of medicine; Major Thomas H. Williams Jr., Montgomery, urologist; captains Frederick H. DeVane and James C. Denton, Birmingham, orthopedic surgeons; and Capt. Daniel T. Meadows, D.D.S., Birmingham, dental surgeon.

CALIFORNIA

Cancer Mortality.—According to the Los Angeles County branch of the American Cancer Society, cancer claimed the lives of 7,381 men, women, and children in Los Angeles County in 1955, eight times as many deaths as the 952 fatalities from automobile accidents.

Proposed Stanford Medical Center.—Former President Herbert Hoover, honorary chairman of the Stanford Medical Center Fund, recently announced the establishment of the fund and its "first stage" objective, to raise $21,950,000 for development of a medical center on the university campus at Palo Alto. The goal includes 1 million dollars for improving the present Stanford University Hospital in San Francisco. For the new medical center a group of three-story buildings is projected, connected by open walkways on all levels and including a 215-bed teaching hospital, clinics, teaching facilities, and a library. The buildings, to be erected on a 40-acre campus site at a cost of $14,450,000, will comprise about 525,000 sq. ft. Endowment funds of $6,500,000 plus the 1 million dollars for remodeling of the present Stanford hospital, comprise the total stage-one goal of $21,950,000.

Funds already available total nearly 4 million dollars, including gifts and bequests of about 2 million dollars and over $500,000 from state and federal agencies to help construct a rehabilitation center unit. A grant of 1 million dollars from the Commonwealth Fund of New York is also included in the sum on hand, although it actually will not be received until matched by gifts from West Coast donors. A long-term stage-two fund-raising effort of equal magnitude, to be made following completion of stage one, will finance further development of the medical center program, build residences for its students, and provide it with adequate endowment.

On completion of the medical center's Palo Alto–Stanford hospitals, combined for economics in construction and joint operation, the city hospital will occupy one 226-bed wing of the building, while the other wing will comprise the Stanford teaching hospital. Additional teaching facilities will be afforded by the 1,000-bed Veterans Administration Hospital to be built on Stanford land. Scheduled for completion by 1959, the VA Hospital was planned at Stanford because of its future proximity to the medical center. A group of local physicians, dentists, and businessmen also have leased 10 acres of nearby Stanford land for construction of a 3 million dollar medical-dental office building, to be ready for occupancy by December, 1957.

CONNECTICUT

Dr. Alice Hamilton Honored.—Dr. Alice Hamilton, aged 87, of Hadlyme, has been named "Medical Woman of the Year" by the Boston chapter, American Medical Women's Association. Dr. Hamilton, in 1910, directed the first comprehensive survey of occupational diseases (in Illinois) and in the following years was a leader in bringing the facts of industrial disease and the need for legislation to protect workers before both state and national governments. She served from 1911 to 1920 as a special investigator of poisonous diseases for the U. S. Department of Labor. Dr. Hamilton served as professor of pathology at Northwestern University Medical School in Chicago, as assistant professor of industrial hygiene at the Harvard Medical School, and as a lecturer at Tufts College Medical School, Boston. She is the author of books and scientific papers, including an autobiography, "Exploring the Dangerous Trades" (1943), and a text, "Industrial Toxicology," now in its second edition.

GEORGIA

Appoint Professor of Psychiatry.—Dr. Erasmus J. McCranie, who has served at Southwestern Medical School of the University of Texas, Dallas, as acting chairman of the department of psychiatry since 1953, has been named a professor in the department of psychiatry at the Medical College of Georgia, Augusta. While in Dallas, Dr. McCranie was also consultant to the Child Guidance Clinic and to the Veterans Administration Hospital, as well as attending psychiatrist at Parkland Hospital.

University News.—The Medical College of Georgia, Augusta, announces receipt of research grants from the U. S. Public Health Service, National Institutes of Health, Bethesda, Md., for the following projects:

Walter G. Rice, associate professor of pathology, (1) Origin, Fate and Nature of Myeloma Proteins; (2) Immunologic Specificity of Human Neoplasms.

Edwin C. Jungck, assistant clinical professor of endocrinology, Effect of "Less-Than-Suppressive" Doses of Testosterone on Testes of Infertile Men.

Chester H. Heuser, Ph.D., professor of microscopic anatomy, Morphological Survey of Early Human Embryos.

John M. Caldwell, professor of psychiatry, Improvement of the Undergraduate Teaching Program in Psychiatry, Including Personnel, Equipment, and Supplies.

Sam A. Singal, Ph.D., professor of biochemistry, Study on the Interrelationship of Phospholipid and Nucleic Acids in Metabolism.

Harland D. Wycoff, Ph.D., assistant professor of oncology and biochemistry, Cholesterol Ester Chemistry and Animal Metabolism.

ILLINOIS

Chicago

Meeting on Medical History.—The Society of Medical History of Chicago will hold an open meeting Dec. 19, at 8 p. m., at the Institute of Medicine (fourth floor, 86 E. Randolph St.). All are welcome. Dr. Aldo A. Luisada, associate professor of medicine, the Chicago Medical School, will discuss, "The Heart in History." Dr. George Halperin, Chicago, will have as his subject, "Theodore Billroth."

Appoint Assistant Dean.—Dr. John A. D. Cooper, associate professor of biochemistry, has been appointed assistant dean of Northwestern University Medical School, with which he has been affiliated since 1943. Dr. Cooper has conducted extensive research in physical biochemistry as applied to medical problems and has directed the medical school radioisotope unit since

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

1948. Dr. Cooper recently directed a course on radioisotope techniques in biology and medicine in Brazil and made a lecture tour of South American universities and scientific societies.

Personal.—Dr. Ralph H. Kuhns, formerly affiliated with the Veterans Administration District Office, Fort Snelling, Minn., has been appointed foreign language expert and psychiatrist for the Veterans Administration regional office in Chicago.——Dr. Jack Metcoff, Evanston, has been named chairman, department of pediatrics and director of pediatric research at Michael Reese Hospital Medical Center. Dr. Metcoff previously served in Boston as chief of the metabolic division of Children's Hospital and as assistant professor of pediatrics and consultant at Harvard Medical School.

MASSACHUSETTS

Personal.—Dr. Charles F. Wilinsky, Brookline, former executive director of the Beth Israel Hospital, Boston, received the 1956 Distinguished Service award of the American Hospital Association at its annual convention in Chicago. The award commends him for his early recognition of the need for coordinated activities between hospitals and health departments and his continued devotion to strengthening this relationship.

Harvard Laboratory Moved to Sweden.—The staff of an entire laboratory of Harvard Medical School and Boston Lying-In Hospital was transplanted to the Karolinska Institute Hospital, Stockholm, Sweden, for a four-month period starting Nov. 1. Under the direction of Claude A. Villee Jr., Ph.D., current studies on changes taking place in embryonic tissue will be expanded in association with the institute staff. Funds for the transportation of laboratory personnel and equipment were made available through the Association for the Aid of Crippled Children.

MINNESOTA

First O'Leary Memorial Lecture.—Dr. Henry E. Michelson, professor of medicine (dermatology) in the University of Minnesota Medical School, Minneapolis, delivered the first annual Paul A. O'Leary Memorial Lecture, "A Consideration of Some Diseases of the Subcutaneous Fat," in Mann Hall, Mayo Clinic, Sept. 8. Dr. O'Leary died on July 20, 1955.

University News.—The University of Minnesota announces the appointment of the following physician members of the Mayo Foundation faculty to full professorships in the graduate school of the university, of which the foundation is a part: Drs. Benjamin M. Black, surgery; Edward N. Cook, urology; Ward S. Fowler, physiology; Haddow M. Keith, pediatrics; and Eric E. Wollaeger, medicine. Appointed to associate professorships are Drs. Albert Faulconer, anesthesiology; George A. Hallenbeck, surgery; Paul R. Lipscomb, orthopedic surgery; Gordon M. Martin, physical medicine and rehabilitation; Donald R. Nichols and Lucian A. Smith, medicine; Charles A. Owen Jr., clinical pathology; and David G. Pugh, radiology. Promoted to assistant professorships are Drs. Donald S. Childs Jr., radiology; Edward C. Clark, Donald W. Mulder, and David de R. Daly, neurology; Henry W. Dodge Jr., neurosurgery; Franklin H. Ellis Jr., surgery; Donald J. Erickson, physical medicine; and Maurice H. Stauffer and William E. Wellman Jr., medicine.

MISSOURI

First Annual Westlake Lecture.—Guest speaker for the first annual Samuel B. Westlake Lecture at the Jewish Hospital medical center, St. Louis, was Dr. Victor Goodhill, clinical professor of surgery (otology) at the University of Southern California School of Medicine, Los Angeles. Dr. Goodhill's lecture on recent advances in the treatment of deafness was delivered Nov. 30. The Samuel B. Westlake Lectures were initiated in memory of Dr. Samuel B. Westlake, for many years an outstanding teacher and director of the department of otolaryngology at Jewish Hospital. They are being made possible by a fund established by Dr. Westlake's patients and friends, to assist in the development of teaching and research facilities at Jewish Hospital for the study of diseases of the ear, nose, and throat.

Personal.—An award for outstanding work in gerontology was presented recently to Dr. Edmund V. Cowdry of Washington University School of Medicine, St. Louis, at a meeting of the Gerontological Research Foundation in St. Louis.——Dr. John P. Wyatt, professor of pathology, St. Louis University School of Medicine, recently spent two months at Scotland Yard, London, as a guest investigator with the coroner system. Dr. Wyatt, who is chief coroner's pathologist for St. Louis County, conducts a training program in the department of pathology at the school of medicine in which graduate students receive instructions in medicolegal pathological investigations.——Dr. Sidney Goldring, Clayton, instructor in neurosurgery, Washington University School of Medicine, St. Louis, has been appointed director of the newly created department of neurosurgery at the Jewish Hospital of St. Louis.

NEW YORK

Dr. Gardner Goes to Yale.—Dr. Lytt I. Gardner, professor of pediatrics, State University of New York College of Medicine in Syracuse, has been appointed professor of pediatrics at the Yale University School of Medicine, New Haven, Conn. Dr. Gardner formerly was affiliated with the Massachusetts General Hospital, Boston; the University of North Carolina School of Medicine, Chapel Hill; and Johns Hopkins University School of Medicine, Baltimore.

Psychiatric Training Program.—The Albany Medical College of Union University, having received grants totaling $22,098 from the U. S. Public Health Service for postgraduate teaching and training of psychiatrists, plans to increase the number of its resident psychiatric trainees from five to eight. A $10,000 increase in the yearly contribution of the Public Health Service to the support of the medical college's undergraduate teaching program in psychiatry will enable the psychiatric department to have one additional instructor and will also benefit residents in psychiatry at the Albany Veterans Administration Hospital, since their third year of training is spent at Albany Medical College.

New York City

Personal.—King Gustaf of Sweden, through the Consul General Erik Kronvall, recently decorated Dr. Harry C. W. S. DeBrun as Knight of Nordstjernan (North Polar Star).

Tumor Clinic Conference.—Dr. Oscar Auerbach, chief, laboratory service, Veterans Administration Hospital, East Orange, N. J., will present "Changes in the Bronchial Epithelium in Its Relationship to Smoking and Cancer of the Lung" at the Harlem Hospital, Dec. 19, 10:45 a. m.

Lecture by Dr. Pasteur Vallery-Radot.—Dr. Pasteur Vallery-Radot, professor of clinical medicine, Faculty of Medicine, University of Paris, France, will deliver the Dr. I. C. Rubin Lecture, "Allergic Manifestations of Interest to the Gynecologist," at 8:30 p. m., Dec. 19, at the Mount Sinai Hospital.

Dr. Hunt Goes to Utah.—Dr. Carlton C. Hunt Jr., professor of physiology, Einstein University, has been appointed head, department of physiology, at the University of Utah College of Medicine, Salt Lake City. He succeeds Horace W. Davenport, Ph.D., who has assumed similar duties at the University of Michigan in Ann Arbor.

Director of Physiology-Pharmacology Department.—Dr. David Lehr, director, department of pharmacology, has been appointed director of the newly combined department of physiology and pharmacology at New York Medical College, Flower-Fifth Avenue Hospitals. Before coming to the college in 1941, Dr. Lehr was on the faculty at the University of Vienna Medical School in Austria, and at the Royal University of Lund in Sweden. Dr. Lehr recently presented a paper at the International Physiological Congress in Brussels on his research with experimental arteriosclerosis. He is chairman of the research committee of the New York Medical College–Metropolitan Medical Center; associate attending physician at Flower–Fifth Avenue Hospitals; and visiting physician at Metropolitan and Bird S. Coler hospitals.

NORTH CAROLINA

Psychiatric Center.—The University of North Carolina School of Medicine, Chapel Hill, announces that an estimated $300,000 building program for the Psychiatric Center of North Carolina Memorial Hospital is scheduled to begin late this year. According to Dr. Robert R. Cadmus, director of the hospital, 50% of the funds required for the project will be supplied by the federal government through the North Carolina Medical Care Commission and the remainder by the state. Plans for the center include laboratories, offices, treatment rooms for the outpatient department, and an auditorium.

University News.—Dr. Walter R. Benson, formerly assistant professor of pathology, University of Louisville (Ky.) School of Medicine, has been appointed to the same post at the University of North Carolina School of Medicine, Chapel Hill.——Dr. Sydenham B. Alexander, clinical assistant professor of medicine, University of North Carolina School of Medicine, Chapel Hill, has been named assistant administrator of the division of health affairs of the University of North Carolina. During World War II, Dr. Alexander was on destroyer duty in the Pacific and during the Korean emergency was chief of diagnostic services of the U. S. Naval Hospital in Portsmouth, Va.

OHIO

Fellowship in Aviation Medicine.—The Air Line Pilots Association, with headquarters in Chicago, has established a $7,200 fellowship in aviation medicine at Ohio State University, Columbus, said to be the first civilian institution to offer graduate training in this specialty. The grant will provide for two years of graduate study.

PENNSYLVANIA

Memorial to Dr. Flick.—Leadership by the late Dr. Lawrence F. Flick in the fight against tuberculosis was honored at a "Dr. Flick Day" program at Carrolltown, Aug. 11, one day after the 100th anniversary of his birth there. A memorial was unveiled, showing a likeness of the medical pioneer with a list of his accomplishments. The bas-relief is flanked by the double-barred cross shown on the Christmas seal. The principal speakers were Dr. Otis L. Anderson, assistant surgeon general, Public Health Service; Dr. Berwyn F. Mattison, Harrisburg, Pennsylvania secretary of health; and Dr. Julius L. Wilson, director, Henry Phipps Institute, Philadelphia. Dr. Flick founded the Pennsylvania Society for the Prevention of Tuberculosis, now the Pennsylvania Tuberculosis and Health Society; was prominent in establishing the Rush Hospital for Consumption and Allied Diseases in Philadelphia; organized the Free Hospital for Poor Consumptives; and helped to establish the Henry Phipps Institute and the National Association for the Study and Prevention of Tuberculosis, now the National Tuberculosis Association. A message from President Eisenhower, accepted by Dr. Lawrence F. X. Flick III, grandson of the late Dr. Flick, read in part: "Largely through the pioneering efforts and dynamic leadership of Dr. Flick, the national movement to combat tuberculosis was initiated. He fought to arouse public interest and organize a crusade against a disease that for centuries has been a plague of mankind."

Philadelphia

Hospital News.—The city-owned Philadelphia General Hospital is featured in a 24-page article in the July issue of *Resident Physician* magazine. The article is the ninth in a series on major medical centers of the United States.

Appointed Professor of Ophthalmology.—Dr. John S. McGavic, who recently resigned as pathologist and chief of laboratories at the Wills Eye Hospital, has been appointed professor of ophthalmology, Temple University Medical Center, where he served as professor of clinical ophthalmology from 1947 to 1950. He was formerly professor of clinical ophthalmology at the University of Pennsylvania Graduate School of Medicine, chief, ophthalmology service, Pennsylvania Hospital, and assistant ophthalmologist at the Memorial Hospital for Cancer and Allied Diseases in New York City. He is in charge of the ophthalmology service at Bryn Mawr Hospital.

Pittsburgh

Mellon Institute Appoints Research Director.—Paul J. Flory, Ph.D., professor of chemistry and acting chairman, department of chemistry, Cornell University, Ithaca, N. Y., was recently chosen by the Mellon Institute of Industrial Research as executive director of research.

UTAH

University News.—The University of Utah College of Medicine, Salt Lake City, announces that Dr. Maxwell M. Wintrobe, head, department of internal medicine, was recently given a three-months' leave of absence in the Far East on a Fulbright Lectureship with headquarters in India.——Norman Weissman, Ph.D., formerly of the State University of New York College of Medicine, recently became associate professor of pathology, and Dr. Julien L. VanLancker, from Louvain, Belgium, was named assistant professor of pathology.——Dr. Erik L. Noach, associate professor of pharmacology, State University of Leiden, Holland, is spending a research fellowship year in the department of pharmacology.——Dr. Yoshitoshi Kasé, assistant professor, department of chemicopharmacology, faculty of pharmacy, University of Kumamoto, Japan, is spending a research fellowship year in the department of pharmacology, working on central respiratory mechanisms.

GENERAL

Award to Dr. Elvehjem.—Conrad A. Elvehjem, Ph.D., dean, graduate school, University of Wisconsin, Madison, was recently named the 1956 recipient of the Charles F. Spencer award of the Kansas City section, American Chemical Society. The award includes a medallion and a $500 honorarium. Dr. Elvehjem, who with his co-workers showed that nicotinic acid was the specific antipellagra vitamin, is a member of the A. M. A. Council on Foods and Nutrition.

Gordon Research Anniversary Dinner.—A dinner to mark the silver anniversary of the founding of the Gordon Research Conferences of the American Association for the Advancement of Science will be held at the Hotel Commodore, New York City, Dec. 27, during the annual meeting of the association. The principal speaker will be Nobel prize winner Glenn T. Seaborg, Ph.D., whose topic will be "The Future Through Science." Reservations, at $10 per person, may be made by writing to W. George Parks, Ph.D., Director, Gordon Research Conferences, University of Rhode Island, Kingston.

Awards for Handicapped Service.—According to the International Society for the Welfare of Cripples and the Albert and Mary Lasker Foundation, three Albert Lasker awards for outstanding achievement in the development of services for the physically disabled will be presented at the seventh World Congress of the society in London, July 24, 1957. The awards, made by the foundation through the society every third year for internationally significant individual and group accomplishments, consist of $1,000 each and a silver statuette of the Winged Victory of Samothrace. Dr. Henry H. Kessler, West Orange, N. J., will be chairman of the Lasker awards committee.

Meeting on Premedical Education.—A symposium, "Problems in Premedical Education," will be presented in the auditorium of Cornell University Medical College, New York, Dec. 29, by Alpha Epsilon Delta fraternity, with the co-sponsorship of the American Association for the Advancement of Science section C-chemistry, F-zoological sciences, N-medical sciences, and Beta Beta Beta Biological Society, and in conjunction with the annual meeting of the American Association for the Advancement of Science. All persons interested in premedical education are invited to attend. Physicians participating in the program will include William N. Hubbard Jr., Lawrence W. Hanlon, E. Hugh Luckey, New York City; and George E. Miller Jr., Buffalo.

Discontinue Shipping Medical Books to Korea.—The American-Korean Foundation and the U. S. Army Medical Service have announced the discontinuation of their joint project of shipping medical books contributed by individual physicians, medical schools, hospitals, and state and local medical societies to Korea

Books should not be sent to the Sharpe General Depot as in the past, because facilities no longer exist for packing and transshipping contributions to Korea. In making the announcement, Dr. Howard A. Rusk, chairman, American-Korean Foundation said, "The response of physicians and medical groups throughout the country for our appeal for books for Korean medical schools has been so generous that further contributions are not needed." As a result of this program, Dr. Rusk stated, over 76 tons (valued at $75,000) of medical texts, references, and periodicals have been shipped to Korea for distribution to Korean medical schools.

International Medical Film Program.—The international medical film program, a new feature for the A. M. A. Annual Meeting in New York City next June, is creating interest abroad. The many applications now coming in indicate an extensive program of medical films made in other countries. The aim of the program is to bring before the doctors who attend the New York meeting outstanding motion pictures produced abroad dealing with many aspects of medical science. This feature is in support of the people-to-people program that President Eisenhower launched this summer and in which the medicine and health professions are cooperating under the chairmanship of Dr. Louis H. Bauer, secretary general of the World Medical Association, New York. Although the film program is not competitive, a certificate of participation will be awarded to each film of distinction selected for showing. In connection with this program, which will be held at the Barbizon Plaza Hotel in New York next June 3-7, a discussion is planned on the problems of a freer international medical film exchange. Representatives of all countries interested in dissemination of medical knowledge by the film medium are invited. Special social events will also provide an opportunity for the participants to meet informally and discuss problems of mutual interest. The film program will be scheduled to permit participants to visit scientific exhibits and other programs, including color television, as guests of the A. M. A. Applications and information may be obtained from the American Medical Association, Motion Pictures and Medical Television, 535 N. Dearborn St., Chicago 10.

Lalor Faculty Awards.—The Lalor Foundation announces the availability of 40 awards to college and university staff and faculty members for research in the biological sciences for the summer of 1957. The awards for advanced study and research employing chemistry or physics to attack problems in any field of biology may be carried on at any institution of the award-holder's choice. The upper age limit for appointment is 40 years. The awards will usually not exceed $900 for a single man or woman, $1,100 for a married person working at his home institution, and $1,250 for a married person whose principal program is at another institution. Transportation and other expenses are for the account of the award holder. Inquiries should be addressed to the Director of the Lalor Foundation, 4400 Lancaster Pike, Wilmington 5, Del. The final date for the receipt of completed applications is Jan. 14, 1957.

FOREIGN

Residency Posts for Doctors from India.—The Indian Medical Association requests offers from recognized U. S. hospitals for residency and internship posts in all specialties for doctors from India, men and women with a good command of spoken and written English, specially selected for graduate training in U. S. hospitals for the session commencing July, 1957. The hospitals must be approved by the U. S. State Department for the exchange-visitor program. Interested hospitals are requested to communicate direct by air mail to the Honorary Secretary, Indian Medical Association, "Hanging Bridge," Daryaganj, Delhi, 7, India, giving offers of posts and the terms of appointment, including maintenance, stipend, and the allotted number for the exchange-visitor program.

Congress on Occupational Health.—The 12th International Congress on Occupational Health will convene July 1-6, 1957, in Helsinki, Finland, to discuss industrial noise, evaluation of invalidity, industrial hygiene norms, and cardiacs and work. Persons who wish to present original scientific papers on these or on any other topics are invited to notify the organizing committee before March 1, 1957, giving the title of the paper and a summary of not more than 200 words in English and French. The Nicolò Castellino prize, 3 million lire (approximately $4,800), will be awarded for the first time at the congress for the most outstanding investigation in the field of occupational health by a research worker, who must be under the age of 35 years and who is not the holder of a university chair. Details can be obtained from Directors of Nicolò Castellino Prize. The University. Naples, Italy. The congress will also have a competition for films concerned with occupational medicine and hygiene (accident prevention films do not qualify for the competition). There will be two classes, one for research and documentary films and the other for popular films for lay audiences. Films may be 16 or 35 mm., in color or black and white, with or without sound track, and must not exceed 20 minutes. Films must be received no later than May 15, 1957, by the Organizing Committee of the Congress at Työterveyslaitos, Haartmaninkatu 1, Helsinki-Töölö. Entries must state by whom the film has been planned, produced, and financed. Information relating to the congress may be had on application to the Organizing Committee, Chairman Dr. Leo Noro and Secretary General Dr. Pentti Sumari.

EXAMINATIONS AND LICENSURE

American Board of Anesthesiology: *Part I.* Various locations, July 19. Final date for filing application is Jan. 19. *Oral.* Asheville, No. Car., Mar. 24-29. Sec., Dr. Curtiss B. Hickcox, 80 Seymour St., Hartford 15, Conn.

American Board of Dermatology: *Written.* Several cities, June 27. *Oral.* Baltimore, Oct. 11-13. Sec., Dr. Beatrice Maher Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *Written.* Oct. 21. *Oral.* New Orleans, Feb. 4-8; Boston, April 3-6. Final date for filing application is Jan. 2. Chicago, May 27-29; San Francisco or Los Angeles, September. Final date for filing application is Feb. 1. *Subspecialties. Gastroenterology.* Philadelphia, April 5-6. Final date for filing application is March 1. Exec. Sec., Dr. W. A. Werrell, 1 West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

American Board of Obstetrics and Gynecology: *Part I.* Various cities of the United States, Canada, and military centers outside the Continental United States, Feb. 1. Candidates must submit case reports to the office of the Secretary within thirty days of being notified of their eligibility to Part I. The cases must be prepared in the manner described in the Bulletin of the board with a duplicate index list. *Part II.* Chicago, May 16-25. Request for reexamination in Part II must be received prior to Feb. 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6, Ohio.

American Board of Ophthalmology: *Written.* Jan. 21. Final date for filing application was July 1. *Oral.* New York, May 23-27; Chicago, Oct. 7-11. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland 9, Maine.

American Board of Orthopaedic Surgery: *Oral. Part II.* Chicago, January 1957. Final date for filing application was Aug. 15. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

American Board of Otolaryngology: Chicago, Oct. 7-11. Final date for filing application is April. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pathology: *Oral and Written. Pathologic Anatomy and Clinical Pathology.* Washington, April 4-6. Final date for filing application is March 1. Sec., Dr. Edward B. Smith, 1040 West Michigan St., Indianapolis 5.

American Board of Physical Medicine and Rehabilitation: *Parts I and II.* New York City, June 8-9. Final date for filing application is March 1. Sec., Dr. Earl C. Elkins, 200 First St., S.W., Rochester, Minn.

American Board of Plastic Surgery: *Entire Examination.* Philadelphia, May 4-6. Final date for filing case reports is Jan. 1. Corres. Sec., Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8.

American Board of Preventive Medicine: *Oral and Written. Public Health.* Schools of Public Health, April 11-13. *Aviation Medicine.* Denver, May 9-11. *Occupational Medicine.* St. Louis, April 26-28. Sec., Dr. Thomas F. Whayne, 615 North Wolfe St., Baltimore.

American Board of Proctology: *Oral and Written. Parts I and II.* September. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

American Board of Psychiatry and Neurology: *Oral.* New Orleans, Mar. 18-19. Final date for filing application was Sept. 10. Sec., Dr. David A. Boyd, Jr., 102-110 Second Ave., S.W., Rochester, Minn.

American Board of Radiology: Tampa, April 1-6. Final date for filing application is Jan. 1. Washington, Sept. 23-28. Final date for filing application is June 1. Sec., Dr. B. R. Kirklin, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Part II.* Los Angeles, Jan. 14-15; San Francisco, Jan. 17-18; Houston, Feb. 18-19; Nashville, Mar. 11-12; Boston, April 8-9, and New York, June 10-11.

American Board of Urology: February 1957. Sec., Dr. William Niles Wishard, 1711 N. Capital Ave., Indianapolis 7.

Board of Thoracic Surgery: *Written.* Various centers throughout the country, February 1957, and the closing date for registration is Dec. 1, 1956. Sec., Dr. William M. Tuttle, 1151 Taylor Ave., Detroit 2.

GOVERNMENT SERVICES

ATOMIC ENERGY COMMISSION

Dr. Bruner Appointed to AEC.—Dr. Harry D. Bruner has been appointed chief of the medical branch of the division of biology and medicine, Atomic Energy Commission, succeeding Dr. Roy E. Albert, who has accepted a research and academic appointment at George Washington University, Washington, D.C.

Dr. Bruner received an M.D. from the University of Louisville, Ky., and a Ph.D. in physiology from the University of Chicago. He was chairman of the pharmacology department at the University of North Carolina from 1947 until 1949, when he became chief scientist, medical division, Oak Ridge Institute of Nuclear Studies in Tennessee, serving until 1952, when he was appointed chairman of the department of physiology at Emory University, Ga.

As chief of the medical branch, Dr. Bruner will be responsible for administering the commission's medical program, including research on the mechanism, diagnosis, and treatment of radiation injury and the application of radioisotopes to the diagnosis and treatment of disease; research on toxicity of chemical compounds used in the atomic energy program; and the training of industrial physicians.

ARMY

Proposed Ionizing Radiation Center.—The proposed U. S. Army Ionizing Radiation Center will be located at the Sharpe General Depot, Stockton, Calif. The experimental center will include a nuclear reactor, built by the Atomic Energy Commission, which, together with related equipment, will cost about $3 million dollars. The reactor will be a source of intense gamma radiation.

The center will investigate the use of ionizing radiation in the preservation of foods and conduct other projects of interest to the Department of Defense. The processing area will be designed so that a large variety of products may be handled and major modifications in processing lines may be effected. The Quartermaster Research and Development Command at Natick, Mass., will direct the operations of the center.

The Quartermaster Food and Container Institute, Chicago, is conducting the over-all Quartermaster Corps research and development program in the field of radiation preservation of food. This program includes contracts with 16 universities and with research institutes and industrial concerns throughout the country. The food processed through the Army Ionization Radiation Center will be used in part for support of these contracts. It is expected that work will commence during this fiscal year and that the center will be in operation late in 1958.

NAVY

Reserve Officers Transfer to Regular Navy.—The following naval reserve medical officers have recently been commissioned in the Medical Corps of the regular Navy: Commander D. L. Custis, lieutenants J. D. Manhart, J. L. Glass, J. L. Reeder, T. R. Kleh, F. R. Walton, R. D. Cordier, C. E. Carlton Jr., F. M. Wolfe, R. E. Donahue, V. H. Fitchett, J. R. Williams, M. F. Sokoloff, C J. Philbrick, E. H. Lanphier, C. J. McGrew Jr., J. D. Gross, J. W. Bickerstaff Jr., E B. McMahon, E. P. Ellis Jr., T. S. Dunn Jr., Robert A. Smith, Samuel O. Cornwell, John H. Mazur, John F. Heath, H. R. Schumacher, David E. Cowan, and Erwin L. Burker, and Lieut. Commander R. D. Workman.

Dr. Selye's Address at Navy Hospital.—Dr. Hans Selye, director, Institute of Experimental Medicine and Surgery at Canada's Université de Montreal, addressed the staff of the U. S. Naval Hospital, Corona, Calif., Nov. 13. Also attending the lecture were students and faculty members of the University of California interested in Dr. Selye's work on stress.

Personal.—Dr. Howard T. Karsner, medical research advisor to the surgeon general of the Navy, has been elected a member of the New York Academy of Sciences.

Navy Crew Commended.—Hospital corpsmen and nonmedical personnel of the USS *Salem* were commended by the commanding officer for excellent performance of duty in handling the injured personnel of the USS *John R. Pierce* when on Oct. 1, 1956, a 5-in. gun-mount exploded aboard the destroyer, injuring 13 of its crew members. The *Pierce* transferred the injured men via high line to the *Salem*, whose medical personnel and other crew members cared for them and further transferred them to a nearby airfield for evacuation to a naval hospital. The acting surgeon general, Rear Adm. Bruce E. Bradley, added his congratulations to the men who performed their duty so outstandingly.

Captain Poos Awarded Gorgas Medal.—For contributions in preventive medicine while officer-in-charge, U. S. Navy preventive medicine unit no. 6, Hawaii, Capt. Robert S. Poos, Medical Corps, retired, received the Gorgas medal at the annual meeting of the Association of Military Surgeons in Washington, D. C., in November. Dr. Poos was selected for the award for his work relative to poliomyelitis among naval personnel and their dependents in Hawaii and to the use of Salk poliomyelitis vaccine under epidemic conditions. Dr. Poos, a native of Missouri, and Mrs. Poos reside at Claremont, Calif.

Guam Hospital Staff Commended.—At the recent third special session of the Guam Legislature, the medical department staff of the U. S. Naval Hospital on Guam were commended for their extraordinary services in furnishing supplementary medical care and consultations to the people of Guam at their Memorial Hospital. Capt. Frank P. Kreuz, M. C., U. S. Navy, is commanding officer of the Naval Hospital at Guam.

Medal Awarded to Navy Doctors.—The Association of Military Surgeons at their annual convention in November in Washington, D. C., awarded the Founders medal for 1956 to Capt. Eugene V. Jobe, M. C., U. S Navy, and Capt. Walton L. Jones, M. C, U. S. Navy. The Founder's medal is given for outstanding contribution to military medicine and meritorious service to the association. Captains Jobe and Jones are on duty in Washington, D. C., at the Navy's bureau of medicine and surgery.

AIR FORCE

New Air Force Medical Officers.—The U. S. Air Force Medical Service announced that the following 24 physicians were tendered regular appointments in the Air Force about Oct. 1, 1956. Albert S. Anderson, Dewey J. Bailey Jr., Laurence T. Beahan, Edwin A. Bowman, Kenneth P. Carlson, Gerald Davis, Robert M. Dean, William A. Dunnagan, James A. Gorman Jr., Jere D. Guin, John B. Longenhagen, Strother B. Marshall, James W. Mason, Donald E. McNealy, Francis C. Null Jr., John R. Pfrommer, Eldred T. Richey Jr., William W. Rueve, James J. Schubert, Kuno C. Schwarz, W. T. Snodgrass, Dennis J. Sullivan, Charles O. Titus, and Hiroshi Yamauchi.

Personal.—Brig. Gen. Victor A. Byrnes, director, professional services, office of the surgeon general, U. S. Air Force, delivered the Mc Reynolds Memorial Lecture on "Eye Injuries Produced by Atomic Explosion" at the University of Texas, Oct. 31.

VETERANS ADMINISTRATION

New Clinical Investigator Program.—The Veterans Administration, Washington, D. C., has made the following announcement

The needs of the Veterans Administration medical program and the potential of its research and education activities in contributing to the nation's health are such that the VA plans to train selected physicians and dentists whose primary responsibility will be medical research. The candidates must be interested in problems of importance in the care of veteran patients in fields basic to neurology and psychiatry, cardiovascular disease, cancer, degenerative diseases, and problems involving the aging process. Maximum freedom of choice of subject will be allowed within these broad fields. Any physician or dentist is eligible who has completed at least the formal residency training period required prior to American specialty board certification and who because of special interest and aptitude wishes to do full-time research for a period of possibly up to three years.

The clinical investigator will spend at least three-fourths of his time in research. The balance of his time may be spent in teaching and patient care or in whatever professional activity he and his sponsors agree is advantageous for his development. He will be appointed as a full-time member of the Veterans Administration hospital staff, and his official title will be Veterans Administration clinical investigator. He will be entitled to the privileges and benefits of other full-time physicians and dentists, such as insurance and retirement eligibility and annual and sick leave. All clinical investigators will have research as their primary responsibility; they will, in addition, hold suitable clinical appointments on the hospital staff that will enable them to enjoy the privileges of a responsible relation to the patient care program. The clinical investigator will be appointed at intermediate grade. The beginning salary is $8,990 per year. Additional credit will be given for American specialty board certification in accordance with existing regulations.

Candidates are nominated to the VA hospital manager through the VA hospital research committee for approval by the deans committee. From the group of nominees the clinical investigators will be selected by the central advisory committee composed of outstanding educators and investigators. The candidate should submit a *curriculum vitae*, including transcripts of his scholastic record and other information that might help the committee in its evaluation. He should prepare a detailed description of his proposed research program and make a brief statement of his future plans and ambitions. The candidate should select a preceptor who will follow his career throughout the period of appointment. The preceptor may be any person approved by the deans committee, within or without the Veterans Administration. The sponsoring hospital will describe the research and other facilities available for use by the investigator. Additional information and assistance in completing the application should be secured from the deans committee or hospital manager. In making the final selection the central advisory committee will consider not only the qualifications of the candidate but the ability of the hospital to provide an atmosphere conducive to his development.

Selection will be made semiannually for January and July appointment. Applications may be obtained from the manager of the VA hospital of choice. The completed forms are submitted by the deans committee to the Office of the Assistant Chief Medical Director for Research and Education, Veterans Administration, Washington 25, D. C. The candidates will be notified of their selection by the chief medical director through the hospital manager.

Awards to Employees at Fort Lyon Psychiatric Hospital.—The employees of the VA hospital at Fort Lyon, Colo., received an award of $4,360 presented by Dr. William S. Middleton, VA chief medical director, in a ceremony at the hospital on Nov. 12. Each of the 436 employees of the hospital who were on duty six months or more as of May 2 received $10 and a certificate of commendation for superior performance and teamwork. Dr. Middleton said that the Fort Lyon Hospital had received the Achievement Award of the Year from the American Psychiatric Association for showing the most improvement in patient care of any hospital in the United States during 1955. The VA's award demonstrates, it was said, that modern psychiatric care can be made available at an isolated station operating with a limited but devoted medical staff. Dr. Howard P. Morgan is the hospital manager.

Fort Lyon, a 781-bed hospital specializing in the care of mentally ill veterans, is located on the site of an old frontier post, later a military fort. The Navy established a tuberculosis hospital there in 1906 and the VA took it over in 1922.

Hospital News.—Dr. Alvin Turken, Tarrytown, N. Y., addressed the staff of the Veterans Administration Hospital at Northport, L. I., Oct. 30, on "Application of Orthopedic Measures in Neuro-Psychiatric Problems."

PUBLIC HEALTH SERVICE

New Program to Increase Research Manpower.—The Public Health Service announced Nov. 20 five-year research fellowship awards to 44 scientists in 29 universities and medical schools in 20 states, the District of Columbia, and Canada. The awards are the first in a new federal program designed to increase manpower for research in the basic medical sciences. Recipients are scientists who have completed their doctor's degrees in biochemistry, pharmacology, physiology, microbiology, pathology, and the psychological sciences. Each fellow will receive a salary not to exceed $10,000 yearly, plus up to $2,000 to defray part of the expenses of his research. The salary level is set by the institution to approximate the salaries of scientists doing similar research and teaching as members of the regular faculty. These fellowships will permit recipients to continue their research activities. Concurrently, the sponsoring institutions will assign appropriate teaching responsibilities so that fellows may qualify for full-time academic positions at higher levels.

The new program results from over two years of study by the Public Health Service, aided by experts and the advice of medical school deans and heads of university departments concerned with research and teaching in the basic medical sciences. In citing the need for senior fellowships, the surgeon general said a survey revealed that for the current year over 200 authorized and budgeted positions on the faculties of medical and basic science schools are unfilled. Included are 55 professorships, 52 associate professorships, and 79 assistant professorships. He added that about the same number of vacancies existed last year.

The Public Health Service will award between 40 and 50 new fellowships annually until about 250 have been given by the fifth year. Thereafter the program will be maintained at this level until the national deficiencies have been met. The total cost of the first year of the program will be about $500,000.

Aid to Build Sewage Treatment Works.—The Public Health Service is ready to act on applications for federal grants to help build sewage treatment facilities, and criteria for determining the propriety of federal aid have been established.

Congress appropriated 50 million dollars for the new construction-grants program during the current fiscal year. The new act limits individual grants to 250 thousand dollars or 30% of the estimated cost of the project, whichever is less. Among other conditions, to be eligible for a federal grant a project must be part of a comprehensive water pollution control program developed cooperatively by the Public Health Service, other federal agencies, state and interstate agencies, municipalities, and industries. The program list now includes about 10,000 municipalities. In addition, eligible projects must be in conformity with the state water pollution control plan and must have been certified by the state water pollution control agency as entitled to priority over the other eligible projects on the basis of financial as well as water pollution control needs.

Annual Survey of Illness.—Forrest E. Linder, Ph.D., has been named director of a new Public Health Service program to survey the nature and extent of illness and disability in the population each year. The survey, authorized by the past Congress, also will include data on medical services received by the ill and disabled. The last previous federal survey of this type was in 1936. The Public Health Service plans to use scientific door-to-door sampling techniques to obtain accurate information on the amount, distribution, and effects of illness and disability, and the services received because of such conditions.

Dr. Linder, a native of Waltham, Mass., comes to the Public Health Service from the United Nations statistical office. He received his doctor of philosophy degree from the State University of Iowa. Prior to his work with the United Nations, he was deputy chief of the National Office of Vital Statistics of the Public Health Service.

Personal.—Dr. Donald W. Patrick, director, Clinical Center of the National Institutes of Health, at Bethesda, Md., has been appointed medical officer in charge of the Public Health Service Hospital at San Francisco, succeeding Dr. Kenneth R. Nelson, who is being transferred to Washington, D. C., to be associate chief of the Bureau of Medical Services.—Dr. Edgar B. Johnwick has been appointed medical officer in charge of the U. S. Public Health Service Hospital (National Leprosarium), Carville, La., succeeding Dr. Eddie M. Gordon Jr., newly appointed chief quarantine officer at Fort Monroe, Va., in charge of foreign quarantine activities in the Norfolk and Hampton Roads area. The Public Health Service at Carville, La., is the only institution in the continental United States devoted exclusively to the treatment and rehabilitation of persons with leprosy.

DEATHS

Osgood, Robert Bayley ⊕ Boston; born in Salem, Mass., July 6, 1873; Harvard Medical School, Boston, 1899; John B. and Buckminster Brown professor of orthopedic surgery emeritus at his alma mater; specialist certified by the American Board of Orthopaedic Surgery; past-president of the American Orthopaedic Association and the New England Surgical Society, member of the American Academy of Orthopaedic Surgeons, American Academy of Arts and Sciences, International Society of Orthopaedic Surgery, and the Boston Surgical Society; corresponding member of the Belgian Orthopaedic Association and the Australian Orthopaedic Association; honorary member of the British Orthopaedic Association, Italian Orthopaedic Association, and the Scandinavian Orthopaedic Association; fellow of the American College of Surgeons; veteran of World War I; *honorary surgeon and formerly* chief of staff, orthopedic service, Massachusetts General Hospital; consultant at the Children's Hospital, where he was formerly chief of staff, orthopedic service; died Oct. 2, aged 83.

Behan, Richard Joseph ⊕ Pittsburgh; born in Pittsburgh June 1, 1879; Western Pennsylvania Medical College, Pittsburgh, 1902; served on the faculty of his alma mater; past-president of the Allegheny County Medical Society; member of the Pittsburgh Surgical Society; fellow of the International College of Surgeons and the American College of Surgeons, of which he was an ex-governor; served in the Red Cross during the Serbian-Bulgarian War in 1913 and in recognition of his services was decorated by King Peter of Serbia; veteran of World War I; author of several books; from 1915 to 1939 chest surgeon at the Leech Farm Sanatorium; from 1922 to 1938 on the staff of the Pittsburgh City Home and Hospitals in Mayview, Pa.; from 1939 to 1942 medical director of the Allegheny County Institution District Hospital in Woodville; on the staff of St. Joseph's Hospital and Dispensary, where he died Oct. 8, aged 77, of a cerebral accident.

Jones, Isaac Hampshur ⊕ Los Angeles; born Sept. 26, 1881, University of Pennsylvania Department of Medicine, Philadelphia, 1906; member of the Association of Military Surgeons of the United States, American Laryngological, Rhinological and Otological Society and the American Otological Society, past-president of the Pacific Coast Oto-Ophthalmological Society; specialist certified by the American Board of Otolaryngology; fellow of the Aero Medical Association; during World War I served on recruiting duty for the newly-created aviation section of the Signal Corps; served abroad, for which he was made a Chevalier of the French Legion of Honor, formerly on the faculty of the University of Southern California School of Medicine; served on the staffs of the Los Angeles County Hospital and the Hospital of the Good Samaritan; died Sept. 7, aged 74, of carcinoma of the parotid gland with metastases

Miller, Felix Perryman ⊕ El Paso, Texas; born in Coryell Aug. 20, 1874; University of Texas School of Medicine, Galveston, 1899; formerly a pharmacist; specialist certified by the American Board of Surgery; member of the American College of Chest Physicians and the American Association for the Surgery of Trauma; fellow of the International College of Surgeons and the American College of Surgeons, member of the House of Delegates of the American Medical Association in 1930-1931 and from 1935 to 1939, past-president of the Medical Association of Texas and *the El Paso County Medical Society;* served on the county health board, on the staffs of the Southwestern General Hospital, Providence Memorial Hospital, and Hotel Dieu, Sisters' Hospital, consultant, William Beaumont Army and El Paso General hospitals, died Aug. 23, aged 82, of carcinoma of the liver.

Dobbie, Robert Paul ⊕ Buffalo; born in Buffalo in 1895; University of Buffalo School of Medicine, Buffalo, 1917; clinical professor of surgery at his alma mater; member of the American Association for the Surgery of Trauma and the Industrial Medical Association; fellow of the American College of Surgeons; member of the founders' group of the American Board of Surgery; past-president of the Buffalo Academy of Medicine and the Buffalo Surgical Society; for many years senior surgeon for the Republic Steel Corporation and the Donner-Hanna Coke Corporation; on the staff of the Buffalo General Hospital, where he was president of the medical staff and at one time secretary and treasurer; on the staffs of the Children's Hospital and the Edward J. Meyer Memorial Hospital; died in the Buffalo General Hospital Aug. 27, aged 60, of malignant hypertension.

Petty, Wallace Sidney ⊕ Macon, Mo.; born in Millport July 13, 1887; Keokuk Medical College, College of Physicians and Surgeons, Keokuk, Iowa, 1908; *completed a course in public health* at the University of Minnesota, Minneapolis, in 1941; specialist *certified by the American Board of Preventive Medicine,* past-president of the Iowa Public Health Association; in 1942 elected vice-president of the International Society of Medical Health Officers; veteran of World War I; *served as director of the* Woodbury County (Iowa) health unit and the Sioux City (Iowa) Health Department; formerly director of the divisions of local health services and communicable disease control, and state director of health, Nebraska Department of Health; district health officer for the Missouri State Department of Health, died Sept. 9, aged 69, of cerebral hemorrhage.

Wilson, David Alexander ⊕ Greenville, S. C.; born in East Liverpool, Ohio, Feb. 1, 1910; *Ohio State University College of Medicine, Columbus, 1938; specialist certified by the American Board of Surgery; member of the Southeastern Surgical Congress;* fellow of the American College of Surgeons; interned at the Duke Hospital in Durham, N. C., where he served a residency; formerly a resident at the Franklin County Sanatorium in Columbus, Ohio, and the Kent General Hospital in Dover, Del.; served as president of the South Carolina Surgical Society; on the staff of the Greenville General Hospital, member of the board of directors of the Greenville Chamber of Commerce, died Sept. 17, aged 46.

Teveluwe, William Anthony, *Blanco,* Texas; born in Cincinnati July 23, 1877; *Cincinnati College of Medicine and Surgery,* Cincinnati, 1898; *past vice-president of the* Hayes-Blanco Counties *(Ohio) Medical Society;* a draft board physician during World War II, *formerly* practiced in Cincinnati, where he was on the staffs *of the St. Francis* Hospital, Good Samaritan Hospital, *and* St. Mary's Hospital, where he was president of the staff in 1932; served as attending physician at Mount Alverno Home for Boys in Cincinnati, on the staff of the Hospital in the Hills, where he died Sept. 18, aged 79, of cancer of the sigmoid.

Artman, Byron E., Wichita, *Kan.*; Eclectic Medical Institute, Cincinnati, 1888, died Sept. 22, aged 90.

Brown, Elmer Jonathan ⊕ Manchester, N. H., Medical School of Maine, Portland, 1910, member of the American Urological Association; for many years on the staff of the Elliot Hospital died Oct. 6, aged 72, of cerebral hemorrhage.

Bundsen, Charles Albin ⊕ Denver, Gross Medical College, Denver, 1902, veteran of the Spanish-American War, member of the American College of Chest Physicians and the American Trudeau Society, formerly member of the state board of health once decorated by the King of Sweden, for many years on the *staff of the Mercy* Hospital; founder and retired medical director of the Swedish National Sanatorium in Englewood, where he died Sept. 3, aged 83, of arteriosclerosis.

Conliffe, Milton Mitchinson, *Fairmont,* W. Va.; College of Physicians and Surgeons, Boston, 1914, an associate member of the American Medical Association; served on the staff of the Fairmount *General Hospital;* died in a New York hospital Oct 1, aged 71.

Cox, Walter Edward ⊕ Brownsville, Texas; University of Arkansas School of Medicine, Little Rock, Ark., 1912, *served as health* unit director for the state health department; *died Sept. 17,* aged 78, of arteriosclerosis.

⊕ Indicates Member of the American Medical Association.

Dale, Joseph Wilbur ⊕ Chesterton, Ind.; Chicago College of Medicine and Surgery, Chicago, 1910; past-president of the Porter County Medical Society; served on the staff of the Porter Memorial Hospital in Valparaiso; died in Westville Aug. 18, aged 68.

Dixon, Francis Samuel ⊕ Natchez, Miss.; Tulane University School of Medicine, New Orleans, 1932; member of the Southeastern Surgical Congress; fellow of the American College of Surgeons; served as secretary of the Adams County Medical Society; consultant, Natchez Charity Hospital, where he was superintendent; on the staffs of the Natchez General Hospital and the Natchez Sanatorium, where he died Oct. 3, aged 55, of coronary thrombosis.

Fenn, Harry Todd, Mount Dora, Fla.; University of Alabama School of Medicine, Mobile, 1911; member of the Florida Medical Association; died in the Orange Memorial Hospital, Orlando, Oct. 6, aged 69, of cerebral thrombosis.

Fisher, Charles Thompson ⊕ Salisbury, Md.; University of Maryland School of Medicine, Baltimore, 1901; fellow of the American College of Surgeons; past-president of the Wicomico County Medical Society; served on the staff of the Peninsula General Hospital, where he died Sept. 19, aged 77, of heart disease.

Gambacorta, Leopoldo ⊕ Newark, N. J.; Regia Università di Napoli Facoltà di Medicina e Chirurgia, Italy, 1906; on the staff of the Columbus Hospital; died Aug. 23, aged 75, of cerebral hemorrhage.

Garvin, Edward Ralph, Toledo, Ohio; St. Louis University School of Medicine, St. Louis, 1931; veteran of World War II and received a Navy Commendation Ribbon and citation for "meritorious and efficient performance of duty"; on the staffs of the Mercy Hospital and St. Charles Hospital, where he was chief of obstetrics and gynecology and where he died Sept. 19, aged 50, of coronary occlusion with myocardial infarction.

Hackney, Ben Hall, Lucama, N. C.; Medical Department of Tulane University of Louisiana, New Orleans, 1911; died Oct. 2, aged 68, of coronary thrombosis.

Hanks, Ralf ⊕ Fulton, Mo.; St. Louis University School of Medicine, St. Louis, 1926; member of the American Psychiatric Association; past-president of the Missouri Association for Mental Hygiene; interned at St. John's Hospital in St. Louis; formerly resident physician at the Missouri State Hospital No. 4 in Farmington; served as superintendent of state hospitals in St. Joseph, Nevada, and Fulton, where he died Sept. 24, aged 61, of cerebral hemorrhage.

Hannett, James Wallace ⊕ Clyde, N. Y.; Syracuse University College of Medicine, Syracuse, 1908; member and past-president of the New Mexico Medical Society; fellow of the American College of Surgeons; for many years practiced in Albuquerque, N. Mex.; died Sept. 23, aged 74, of carcinoma of the left main bronchus.

Hansen, Roy Theodore ⊕ Hartland, Wis.; Marquette University School of Medicine, Milwaukee, 1918; for many years practiced in Wauwatosa, where for many years he was health officer; served on the staffs of the Johnston Emergency and Mount Sinai hospitals in Milwaukee; died Aug. 21, aged 63, of cardiac decompensation and coronary thrombosis.

Harrell, Forrest Worth ⊕ Jennings, La.; Tulane University School of Medicine, New Orleans, 1922; veteran of World Wars I and II; died Sept. 21, aged 58.

Harris, J. Monroe, Allsboro, Ala. (licensed in Alabama, year unknown); died Aug. 31, aged 88.

Jacobson, Jacob ⊕ Chicago; Loyola University School of Medicine, Chicago, 1919; on the staffs of the Cook County Hospital and St. Joseph Hospital, where he died Oct. 17, aged 60, of acute myocardial infarction.

Jameson, Louis Blair ⊕ Medford, N. J.; Syracuse University College of Medicine, Syracuse, 1909; died in Elizabeth Aug. 2, aged 70, of injuries received in an automobile accident.

Johnson, David Powell, Chicago; Rush Medical College, Chicago, 1902; died Sept. 30, aged 86.

Meuser, Courtland Burgett, Ashland, Ohio; Starling-Ohio Medical College, Columbus, 1912; member of the Ohio State Medical Association; died Sept. 12, aged 70, of yellow atrophy of the liver and infectious hepatitis.

Meyer, Julian Erdreich ⊕ Columbus, Neb.; Jefferson Medical College of Philadelphia, 1917; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; newly installed president of the Nebraska Heart Association, of which he was a trustee from the time it was founded; on the staffs of the Lutheran Hospital and St. Mary Hospital; died Oct. 5, aged 62, of coronary occlusion.

Nadolny, Chester John, Cheektowaga, N. Y.; University of Buffalo School of Medicine, Buffalo, 1926; member of the Medical Society of the State of New York; served as health officer; on the staff of the Millard Fillmore Hospital in Buffalo, where he died Aug. 31, aged 54, of hemorrhage from ruptured esophageal varices and Laennec's cirrhosis.

Naugle, Johnson Edward ⊕ Sterling, Colo.; University of Colorado School of Medicine, Denver, 1910; on the staffs of the Logan County and St. Benedict hospitals; died June 16, aged 71, of coronary disease.

Ober, Bert Frank ⊕ Latrobe, Pa.; Medico-Chirurgical College of Philadelphia, 1906; for many years secretary-treasurer of the Latrobe Academy of Medicine; veteran of World War I; served as secretary of the staff of the Latrobe Hospital, where he died Sept. 27, aged 82, of congestive heart disease.

Quinn, Thomas, Napoleon, Ohio; Toledo Medical College, Toledo, 1909; died Sept. 2, aged 70.

Remley, Arthur Roscoe, Richmond, Mo.; St. Louis University School of Medicine, St. Louis, 1908; died Aug. 27, aged 75.

Sandholdt, John Peter, Moss Landing, Calif.; University of California School of Medicine, San Francisco, 1904; formerly practiced in Monterey, where he was city councilman and mayor; died in Monterey Sept. 24, aged 76, of intestinal obstruction.

Schiffbauer, Hans E. ⊕ Los Angeles; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, Chicago, 1907; associate clinical professor of surgery at the University of Southern California School of Medicine; member of the founders' group of the American Board of Surgery; fellow of the American College of Surgeons; served on the staffs of the California Hospital and the Los Angeles County Hospital; died Sept. 17, aged 73, of heart disease.

Sevenman, George William, San Mateo, Calif.; Cooper Medical College, San Francisco, 1894; an associate member of the American Medical Association; on the staff of the Mills Memorial Hospital; died Aug. 30, aged 82, of myocardial degeneration.

Vanzant, Frances Ralston, Houston, Texas; University of Texas School of Medicine, Galveston, 1926; member of the American Gastro-Enterological Association; fellow of the American College of Physicians; formerly secretary of the Harris County Medical Society; died in the Methodist Hospital Aug. 27, aged 54, of septicemia.

Vernon, Frank Atherton ⊕ Pikeville, Ky.; Medical College of Georgia, Augusta, 1935; member of the Southeastern Surgical Congress; fellow of the American College of Surgeons; veteran of World War II; on the staff of the Methodist Hospital; died Sept. 9, aged 46, of injuries received in an automobile accident.

Vixie, Loren Oliver ⊕ Monterey Park, Calif.; College of Medical Evangelists, Loma Linda and Los Angeles, 1944; died May 5, aged 38.

Wahle, Henry, Oakland, Calif.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, Chicago, 1897; an associate member of the American Medical Association; died in the Providence Hospital July 22, aged 86, of heart disease due to coronary sclerosis.

Walborn, Kenneth Boone ⊕ Fort Worth, Texas; Baylor University College of Medicine, Dallas, 1937; member of the American Academy of General Practice; veteran of World War II; died Sept. 6, aged 45.

FOREIGN LETTERS

AUSTRIA

Reactions of the Infant in the Neonatal Period.—At the meeting of the Society for Pediatrics in Vienna on June 26, Dr. H. Lehndorf stated that a change in the functions of all organs in the newborn infant takes place in the first few days of life. The clinical manifestations that occur unnoticed and without disturbances of the state of health are called reactions of defense; those that occur with symptoms of sickness are called reactions of alarm. In the adaptation phase, hormonal crises are caused by the effort of the newborn infant to be freed from substances transmitted from the mother through the placenta. The most important phenomenon in this phase is the biological allergy of the newborn baby, characterized by such transitory manifestations as erythema, edema, hydrocele, fever, and intestinal disturbances. The hypothesis is proposed that the fetus, which in utero is sensitized by the heterogeneous serum of the mother, during delivery again comes into intimate contact with the maternal blood, thus making for a second injection. This will, after an appropriate interval, produce allergic reactions. The concept of a changed blood morphology in the period of adaptation leads to a better understanding of the phenomena associated with this period. This is shown in the process of erythropoiesis. The elimination of the macrocytes and the creation of a generation of normocytes means a daily change of 20 billion erythrocytes. In addition there is also the decreased value of pleocytosis. The physiological anemia of the newborn infant is regulated by a complicated mechanism, a disturbance of which by shock or allergy will intensify hemolysis and the temporary inhibition of hematopoiesis and will produce the condition of anemia neonatorum transitoria. A physiological neutropenia and rarely a pathological transitory granulocytopenia have been observed in the leukocytopoietic system. A physiological thrombopenia in the first week of life and melena neonatorum have also been observed.

AFRICA

Symposiums on Cancer.—At a symposium on hepatic cancer and related disorders held in August at Makerere College Medical School, Kampala, Uganda, evidence of the high incidence of primary hepatic cancer in native Africans was presented. The incidence varied in different locations, the regions about Dakar, French West Africa, and Lourenco Marques, Mozambique, showing the highest levels. The disease occurs chiefly in men between the ages of 20 and 40, and it runs a rapid course. The gross and microscopic types resemble those seen in Europe and America except that their proportions may be different. The causes are not apparent, but some form of hepatic cirrhosis is usually present in patients with this type of cancer. Although the geographical areas having a high incidence of hepatic cancer also have a high incidence of malnutrition, including cases of kwashiorkor, it was the consensus that the patient with kwashiorkor, who often has an enlarged fatty liver, does not usually have a cirrhotic liver later. Other possible etiological factors were liver parasites, viral hepatitis, and hepatotoxic agents in food or drink.

A symposium on cancer in the native African followed in September at the Louvanian University of Leopoldville in the Belgian Congo. The site distribution of primary cancers in native Africans appears to be different from that in natives of Asia, America, and Europe. Among the tumors that are more frequent in Africa are carcinomas of the salivary glands, liver, and skin (especially the skin of the legs in relation to tropical ulcers), multiple hemorrhagic hemangioma of Kaposi, and reticulum cell tumors. Gastric, pulmonary, and colonic cancers seem to be relatively less frequent. There is some geographical difference in the incidence of various cancers within Africa, and the distribution is different from that found in the American Negro. For example, the great frequency of multiple hemorrhagic hemangioma of Kaposi reported in Uganda and the Congo is not seen in the Senegal at Dakar or in the United States. The participants in the symposium recognized the rich opportunities for studying etiological factors in cancer in this African material and the need for additional data. They recommended that a center be established in Africa for the accumulation and study of this material. A third group of visits and meetings followed immediately at the School of Medicine at Dakar, French West Africa, and included a visit to Pasteur Institute and the Nutrition Study Center. The members of the symposiums from the United States were Drs. A. Cantarow (Philadelphia), H. F. Dorn (Bethesda, Md.), W. S. Hartroft (St. Louis), P. E. Steiner (Chicago), H. L. Stewart (Bethesda), and A. Tannenbaum (Chicago).

DENMARK

Treatment of Lupus Erythematosus.—The claims made for quinacrine in the treatment of lupus erythematosus encouraged Nielsen and Christiansen (*Ugeskrift for læger*, Sept. 6, 1956) to give it an extensive trial. They report that, in a series of 97 patients, the disease was of the discoid type in 81 and of the erythematous type in 16. Most of the patients were treated in the hospital to facilitate the observation of any side-effects of the drug, but 41 were treated as outpatients. Two 100-mg. tablets were given daily for eight days; then 300 mg. was given daily until the skin turned definitely yellow; and then 100 to 200 mg. was given daily for a prolonged period, the smallest total dose being 1.6 gm. and the largest being 49.8 gm. (average 18 gm.). Broadly speaking the results were excellent in 33% and fair in 33%. The results were much the same whether inpatient or outpatient treatment was given, and the patient's sex and the duration of the disease also seemed not to influence the reaction to this treatment, but the prognosis improved markedly with the patient's age, for among the 16 patients over the age of 60, only one failed to get a good result. During an observation period of 12 months after the completion of the treatment, the relapse rate was about 80%. Side-effects were also troublesome, with 5 cases of dermatitis, 16 of dyspepsia, and 8 of hyperhidrosis traceable to the treatment. Because side-effects are reported as being less troublesome with the related chloroquine, this drug was tried. It is hoped that small doses given over a prolonged period may reduce the relapse rate. Freedom from the yellow skin produced by quinacrine is a further advantage of chloroquine. At present quinacrine may be said to be as good as, but not much better than, other drugs hitherto given for lupus erythematosus.

Thrombosis of the Pulmonary Artery.—Dr. K. Iversen undertook a retrospective study of 20 patients in whom thrombosis of the pulmonary artery was found after death (*Nordisk medicin*, Sept. 6, 1956). Most of the patients were elderly and had a variety of cardiopulmonary complaints. The clinical records were therefore bound to present a complex picture from which instructive elements had to be disentangled. The records belonged to a series of about 4,000 autopsy reports, so the incidence of thrombosis of the pulmonary artery in this series was 0.5%. The average age of the patients was 69 years, and in several the thrombi were evidently of long standing. In every case there was a record of dyspnea; dyspnea on exertion was the first symptom noted in 15 patients. All but one had been cyanosed. In 11 there was a history of pulmonary embolism at some earlier date. Most had had prolonged fever refractory to chemotherapeutic and antibiotic agents. Ten had been mentally confused. In 9 the onset of the thrombosis was acute, suggesting pulmonary embolism, and in the remaining 11 it was insidious, manifesting itself as cyanosis and dyspnea. Iversen suggests that a comparison of radiograms taken from time to time in the same patient may give a clue to the correct diagnosis, but he admits that in eight cases clinical evidence on which to found the diagnosis of thrombosis of the pulmonary artery during life was lacking. In such cases the thrombosis may be a terminal phenomenon.

Cancer Register.—Dr. Johannes Clemmesen has described the main activities of the Danish Cancer Register since its foundation in 1942 (*Nordisk medicin*, Oct. 4, 1956). Its task was to collect on a voluntary basis reports on cancer cases from all the hospitals in Denmark and to correlate these reports with the country's death certificates. Cooperation has been assured with the University Genetics Institute in order to facilitate the investigations

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The items in these letters are contributed by regular correspondents in the various foreign countries.

conducted by the register into the influence of heredity on the development of cancer. It has found that heredity does have a certain but limited influence on the development of cancer of the breast. In cooperation with the State Serum Institute, at which a syphilitic register is kept, it was shown that the incidence of cancer of the cervix is abnormally high among prostitutes. The cancer register has also collected data showing that the incidence of carcinoma of the lungs is high in men in Copenhagen, where it was noted for the first time that the lung cancer rate rose as the social status fell. It is calculated that by 1990 the lung cancer rate for men in Copenhagen will be the same as that for all forms of cancer in 1950.

The Prognosis for Patients with Hypertension.—In 1946, Dr. Poul Bechgaard published a report on 1,038 patients with high blood pressure. Since then he has kept in touch with these patients. In *Nordisk medicin* for Sept. 9, 1956, he brought his observations up to date, with a follow-up period of 16 to 22 years. Using the crude death rate in Denmark as a base line (100%) and after excluding patients with renal disease and those who had some fatal disease, such as cancer, at the first examination, he found that the death rate was 238% for his male and 133% for his female patients. With the comparatively good prognosis for women, Bechgaard doubts if it is necessary to enforce strict measures on women with a systolic pressure under 200.

UNITED KINGDOM

Synthetic Detergents.—In 1953 the Minister of Housing and Local Government set up a committee to examine the effects of the increasing use of synthetic detergents. In its report, now published, the committee states that the incidence of skin trouble attributable to synthetic detergents is no higher than that previously due to the use of soap products, alkalies, and allied preparations. Inquiries made by the British Launderers' Research Association have revealed that dermatitis is rare among commercial laundry workers and that no significant increase has occurred since modern synthetic detergents were introduced. Similar investigations made by the Ministry of Health show that among the general population there has been some incidence of cases of dermatitis. Many of them may have been due to the use of unnecessarily strong detergent solutions. In 1951, of just under 10,000 new patients seen at the skin departments of a London and of a provincial teaching hospital, only 143 were suffering from dermatitis attributed to the use of synthetic detergents. The committee states that it has no reason to believe that there has been any increase in incidence since that time.

The manufacturers have reached the same conclusion, based on the results of inquiries among customers and on observation of the incidence of skin irritation among their own employees who have frequent and prolonged occupational contact with synthetic detergents. Users are advised to avoid making up unnecessarily strong solutions and, in any event, to rinse and dry their hands after using these detergents. People with unusually sensitive skins should choose the product best suited to themselves and should continue to use gloves, hand creams, and lotions.

The problem of acute poisoning is not considered serious. The only known case was in the United States, and in this instance a cationic detergent was involved. Most of the synthetic detergents used in England are based on anionic surface agents, and the committee has no evidence to show that these or the "builders" usually incorporated with them would, if swallowed by mistake, have serious effects. The problem of chronic poisoning is more important, as it derives from eating or drinking from crockery imperfectly rinsed after being washed in synthetic detergent solutions or from the drinking water from rivers polluted by sewage effluents containing detergents. Reference is made to an experiment with five commonly used synthetic detergents in which cups were washed in the normal way and drained without rinsing. Sufficient deposits of the detergent remained on the inner surfaces to produce, when the cups were refilled with tap water, concentrations ranging from less than 0.2 to 1.0 ppm of surface-active material. When the cups were rinsed after washing, the concentrations were less than 0.2 ppm—a concentration no greater than that already present in some tap waters before synthetic detergents came into widespread use.

Reference is also made to an investigator who took 1 gm. of sodium alkyl sulfate daily for eight weeks and who also gave, for seven months, 0.2 gm. every two hours in the daytime to a series of patients with gastric ulcer. In neither case was any ill-effect observed. No evidence was found to indicate that anionic or nonionic surface-active agents are harmful in this respect, but observations should be continued for long periods before a final conclusion is reached. Because of the widespread use of synthetic detergents, domestic sewage now contains complex compounds that are not completely destroyed during the treatment of sewage and water. Since the problem of dealing effectively with current synthetic detergents in sewage is considered almost unsolvable, it is essential that the manufacturers investigate the feasibility of replacing the present common types of household synthetic detergents with products of similar efficiency but based on surface-active agents less resistant to known methods of sewage treatment than those used at present. The committee is divided on the question of whether the public interest is sufficiently safeguarded while the recommended research is being carried out.

Emulsifying and Stabilizing Agents.—The Food Standards Committee of the Ministry of Agriculture, Fisheries and Food recommends that the use of emulsifying and stabilizing agents should be subject to statutory regulations and that the control of such agents can best be secured by specifying the substances that may be used. Those agents that are natural constituents of certain foods or are already common ingredients of food apart from their use as emulsifying and stabilizing agents need not be regulated. Apart from these, those recommended for inclusion on an approved list are as follows: superglycerinated fats, synthetic lecithin, propylene glycol alginate, propylene glycol stearate, methyl cellulose, methyl ethyl cellulose, sodium carboxymethyl cellulose, stearyl tartrate, diacetyl tartaric acid esters of superglycerinated fats, monostearin sodium sulfoacetate, and sorbitan esters of fatty acids. The addition of emulsifying and stabilizing agents to milk should not be allowed. Of the approved substances, superglycerinated fats and stearyl tartrate should be allowed in bread. The existing prohibition on the use of thickening substances in cream should be extended to cover reconstituted cream. It is not necessary or practicable to specify limits to the amount of an approved emulsifying or stabilizing agent that may be present in food, but the amount used should always be the smallest quantity consistent with the best commercial practice. Specifications of purity for the approved substances should be drawn up in order to ensure that they are of a high standard of purity when used in food.

Cost of the Welfare State.—At the end of 1955, the Ministry of Pensions and National Insurance was paying war pensions to 870,000 persons; family allowances to 3,250,000 families, consisting of about 8,250,000 children; retirement pensions to 4,500,000; widows' benefits and guardians' allowances to 470,000; and industrial disability pensions to about 130,000. During 1955, new claims for sickness benefits totaled nearly 8 million, for unemployment benefits over 2,250,000, and for industrial injury benefits over 830,000. The combined cost of these and other social benefits being paid by the Ministry of Pensions and National Insurance was at the rate of about 2.38 billion dollars a year. These are some of the facts presented in the annual report of the ministry for 1955. New claims for sickness benefits in 1955 totaled just over 7,900,000, at a cost of over 236 million dollars. It is estimated that 746,000 maternity grants were awarded and that in the same period 287,000 home confinement grants and 196,000 maternity allowances were awarded—at a cost of over 36 million dollars. Prosecutions for alleged traffic in used National Insurance stamps and other misuse of such stamps rose from 243 in 1954 to 320 in 1955. Criminal proceedings for failure to pay contributions and for allied offenses totaled 4,662. Legal proceedings were taken by the minister against 1,014 persons for offenses connected with improperly obtaining benefits; there were convictions in 976 cases.

Alcohol and Body Build.—Evidence suggesting that fat people have a special taste for alcohol is presented by R. W. Parnell (*Internation. J. Alcohol* 1:127, 1955). His conclusions are based on the findings in three different groups. The first group was composed of 265 male Oxford University students about whose drinking habits inquiry was made at the time of routine health examination. Their average age was 22. A correlation of their drinking habits and the findings on somatotyping showed that 25% of the endomorphs took alcohol regularly as compared with less than 5% of the linear ectomorphs. Dominantly muscular men (mesomorphs) occupied an intermediate position. At the age of

22, young men's habits are barely established, but it is reasonably certain that alcohol consumption will not have altered their physique to any material extent. The same trend in drinking was found among 92 male patients, aged 16 to 65 years, in a mental hospital. The third group was composed of 200 juvenile delinquents, in whom the general level of heavy drinking was substantially higher than among the students and mental hospital patients, but the highest proportion of heavy drinkers in this group was also found among the endomorphs.

Deaths due to Anesthesia.—For the first time the annual report of the chief medical officer of the Ministry of Health gives the number of deaths occurring as a result of the administration of anesthetics. There were 562 deaths associated with anesthesia, or about 0.1% of all deaths occurring in the population. In 1949 a plan was initiated by the Association of Anesthetists of Great Britain and Ireland for the reporting of deaths due to anesthesia. A committee was set up to consider such deaths, and it has now issued its report on the first 1,000 reports collected (*Anæsthesia* 2:194, 1956). In almost 600 of the cases, death was associated entirely, or to a large extent, with the administration of an anesthetic. The commonest single cause of death was the inhalation of vomitus. This occurred more often in labor than in surgical operations. In obstetric cases requiring operative treatment, anesthesia has become the commonest cause of maternal death. The report also reveals the frequency of fatalities after the intravenous use of barbiturates. The next commonest cause after death due to inhalation of vomitus is death during the immediate postoperative period due to respiratory obstruction or depression of respiration. Other causes of death listed are endotracheal anesthesia, convulsions, the use of antidotes and analeptics, spinal anesthesia, and deliberate induction of hypotension to minimize bleeding. Lack of skill, inadequate equipment, and insufficient medical or nursing supervision are responsible for many of the deaths. Sometimes in the immediate postoperative period patients are left without efficient suction in the care of a student nurse. Some patients are given powerful drugs without the physician's full appreciation of their effects. Ultimately the prevention of deaths resulting from the administration of anesthetics will depend on better training of anesthetists and nurses.

Blood Groups, Pernicious Anemia, and Duodenal Ulcer.—An editorial in the *British Medical Journal* (2:723, 1956) states that the collection of data from a number of centers shows fairly conclusively that pernicious anemia is commoner in persons of blood group A than in those of blood group O and also perhaps, though the numbers are small, than in those of blood group B. The greater incidence in group A appears in both sexes. An analysis of data, by Dr. C. A. Clarke and co-workers (*Brit. M. J.* 2:725, 1956), from 293 blood relatives with a history of duodenal ulcer gave no evidence to support the hypothesis that a person with blood group O is more likely to have a duodenal ulcer than are his blood relations with blood group A, B, or AB. It will also be a task for the future to ascertain whether the secretor phenomenon is likewise involved in other diseases known to be related to the ABO blood groups, particularly such diseases as carcinoma of the stomach and pernicious anemia. No causal relationship, whether of blood group or of secretion, has been established with any of the diseases mentioned, but, if and when such causal relations become established, it will become a matter of more than theoretical interest to investigate in detail the biochemical mechanism whereby the blood-group substances tend to protect or to damage the intestinal wall or the other tissues of the body. If, as appears likely, many diseases have an incidence that varies according to blood group and if the relation is a causal one, the cumulative natural selective effect on the blood groups is likely to be great. This may be the main reason for the different blood group frequencies found in different populations.

The Old Should Stay at Work.—At the annual meeting of the Association of Industrial Medical Officers, Dr. Andrew Meiklejohn, of Glasgow University, said that planning would soon be one of the major causes of ill-health among workers and others. Recommending continued employment after normal retiring age, he said the decision must be made by the person concerned. "Heaven forbid that we should get any more planning of the worker." Aside from the need for the production put forth by older workers, physicians should stress the fact that the real importance of the continued employment of the older workman is for his own sanity and general well-being. There is no health—physical, mental, social, or moral—in idleness, and idleness is what enforced retirement means for most unskilled laborers in industrial areas. Prof. Sven Forssman, medical adviser to the Swedish Employers' Federation, pointed out that with mechanization heavy work was disappearing. This gave a better chance to the older worker, who, moreover, could compensate for reduced physical strength by experience. A longer lunch period, with a corresponding wage reduction, has been tried with success in some industries.

The Ring Around the Bathtub.—Bacteriological cultures of 20 deposits taken at random by J. A. Boycott from the greasy waterline left after use on the bathtub in the women's ward of a hospital showed viable bacteria in all. These included coliform bacilli, Micrococcus pyogenes var. aureus, Streptococcus faecalis, and species of Neisseria (*Lancet* 2:678, 1956). An investigation was therefore carried out for the best practical method of cleaning bathtubs and basins after use. The following method is recommended, as it makes preliminary cleaning unnecessary and appears to be effective. Water, as hot as can be borne by the bare hand, is run into the tub to between a twentieth and a tenth of its effective content (1 to 2 gal.). To this is added 15 cc. of an approved hypochlorite and detergent sufficient for cleaning purposes. Because some detergents cause a release of chlorine, the hypochlorite and detergent should not be mixed before use. The tub is then washed thoroughly with a clean cloth used for this purpose only and the water allowed to drain out. Subsequent washing with tap water is unnecessary unless there is gross dirt left loose in the tub or unless an excess of detergent has made the tub slippery.

Prefrontal Leukotomy.—Elithorn and Slater in the *British Medical Journal* (2:739, 1956) say that recent correspondence in the *Lancet* and the *British Medical Journal* has shown that there are still widely diverging views on the value of leukotomy in the treatment of mental disorders. Of 103 patients, 66 were glad to have had the operation, 14 regretted it, and 23 were neither glad nor sorry that they had had the operation. The views of 93 relatives were also obtained: 72 thought the patient was better off, 11 thought the patient worse, and 10 thought it had made little difference. Unwelcome changes were reported by 43 patients and 51 relatives. A good result was reported much more often with a standard than with a modified operation. On the other hand, the incidence of bad effects was only slightly higher with the standard operation. It is emphasized that, whoever makes it, the determination of the value of a leukotomy to the patient is subjective.

X-Ray Hazards from TV Apparatus.—There is little danger to the public from x-rays emitted by cathode-ray tubes used in television sets, according to L. B. Bourne (*Lancet* 2:510, 1956). This conclusion is based on the findings in an investigation in which nine men and one woman were exposed for one working week to cathode-ray tubes subjected to voltages up to 20 kv. and monitored for irradiation from x-rays and cathode-ray tubes. In all the tests the results were below the tolerance level specified by the International Commission on Radiological Protection. This safety of television sets is due to the adequate safety standards incorporated in such apparatus. It may, however, become necessary to adopt new standards of protection if changes are made in television receiving equipment.

Candida Organisms in Sputum Specimens.—In order to determine the incidence of Candida species in routine sputum specimens Armstrong and Hall (*Month. Bull. Min. Health* 15:220, 1956) examined 307 specimens: 218 from nine chest clinics, 87 from four sanatoriums and one hospital for infectious diseases, and 2 from general practice. Yeasts were isolated from 195 specimens, or 63.5%. Of the 195 patients whose sputum yielded yeasts, 86 were also known to be excreting tubercle bacilli. All the 12 strains of Candida albicans that were inoculated subcutaneously into guinea pigs proved to be virulent. Since no particular precautions were taken in collecting the specimens, the mouth must be considered the source of some of the strains of yeasts isolated

CORRESPONDENCE

NEUROLOGICAL ILLNESS FOLLOWING POLIOMYELITIS VACCINATION

To the Editor:—The Poliomyelitis Surveillance Unit of the Communicable Disease Center, U. S. Public Health Service, has, since its inauguration in May, 1955, systematically collected information from all states on all aspects of field experience with Salk vaccine. This information is compiled in a weekly or bimonthly mimeographed report that is distributed to health departments, epidemiologists, clinicians, laboratory workers, and others interested in this field.

As one aspect of our national poliomyelitis surveillance program, we have collected data on a number of cases of neurological reactions following poliomyelitis vaccination. These were most recently summarized in our report no. 88. The neurological reactions following vaccination have been diverse in their manifestations. In the group included in report no. 88 there was only one case of myelitis. Since that report we have received several more reports of neurological illnesses in recently vaccinated individuals. Only one of these was a case of transverse myelitis. Both of the cases of transverse myelitis that have been reported to us have occurred in young children.

It is difficult to reach any final evaluation of these reports. However, since over 90 million inoculations of poliomyelitis vaccine have been given since May, 1955, it would be expected that a number of cases of neurological and other types of illness would occur by coincidence in recently vaccinated individuals. The relatively small number of possible complications of this nature combined with their diversity, and in face of the millions of inoculations given, lead us to believe at the present time that there is probably no causal association with the vaccine.

Our channels of reporting for various aspects of our program are primarily through state and local health departments. Since the health departments have no routine method of receiving reports of such peculiar reactions to vaccine, it is probable that we have not heard of all incidents of this type. It would be of great value to us if it could be noted that the Public Health Service is attempting to collect these data on a nationwide basis. We would be most interested in receiving reports of this kind, and these should be addressed to me at the address given below. Practitioners might also be urged to report such instances to their local or state health departments, which would then forward them to us. I would also be happy to answer any queries concerning these cases that are directed to us. Anything The Journal can do along this line to stimulate a more complete reporting on these atypical situations would be a value to us and would be highly appreciated.

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SOCIAL SECURITY

To the Editor:—I should like to point out two errors in the article by Webster and Coffey, "Social Insecurity—The Trap Awaiting the Young M.D.," which appeared in the Sept. 15, 1956, issue of The Journal, page 231. It is stated "you cannot collect both survivors' benefits and retirement benefits. It's one or the other." This is, of course, true. However, no young physician can know which type of benefit he will need, whether he will survive long enough to retire, or whether he will die prematurely. Social security takes care of either eventuality for the single premium. Therefore, the cost of social security should be compared with the cost of commercial survivors' benefits plus retirement benefits, rather than with the cost of each individually, as was done in this article. It is stated "We believe your chances of retiring are less than one in seven . . . let us look for costs of a private [retirement] plan that would pay benefits equaling one-seventh of . . . social security . . . benefits." The cost of such private insurance is naturally found to be lower than that of social security. If I will need such and such a monthly income on which to retire, I will not be able to live on the fraction of that amount determined by the likelihood of my need for it. By such reasoning, my home, which is worth $20,000, should be insured against fire for only $200, since the chance of a house in my community catching fire is only one in a hundred.

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To the Editor:—The issues of The Journal for Sept. 15 and 22, 1956 (pages 231, and 426, respectively), contain a two-part article on social security written by two physicians. The subject of social security is, indeed, pertinent to all physicians in America today. This is so because of a train of events that has led to a situation where we physicians are now the only group of workers in the United States not covered by this program. When one considers the number of physicians compared to the total population, we form a small fraction, and a searching reappraisal of our position might be in order. In making such a reappraisal, some considerations to bear in mind before arriving at a conclusion are as follows: There is no move afoot in either major political party to abolish the social security system; both parties have outlined plans to broaden and strengthen the program. The social security system is underwritten by the United States government, and so every United States citizen is, in turn, an underwriter. Since we physicians are also citizens, we are in a position of underwriting a program from which we derive no benefit. The social security program came into being as a result of legislation. However, the operating methods and details were set up by an advisory committee of citizens, and such a committee has continued to function in an advisory capacity. From the beginning, this committee has included successful and well-recognized executives from the insurance industry. When the annual committee reports of the county medical society are read, one hears, among others, the report of the welfare committee. When this report is read, one learns that there are fellow physicians living in retirement and survivors of deceased colleagues who could well use the benefits of a program such as the social security program offers, yet if they were getting this help they would not be getting charity. In conducting a referendum vote among the physicians as to whether they favor being taken into the social security program as a group, it is unrealistic to include the question as to whether the individual is in favor of inclusion on an optional basis. It is unrealistic to vote on such a question, because no such optional plan would be or could be considered by Congress. It is an inherent feature of the social security program, as it is set up, that it take in blocks of citizens on a compulsory basis. In recent years, doctors have been gaining experience in the operation of insurance plans through their local medical contract bureaus. This experience has taught us what professional insurance underwriters already knew, viz., that, in writing a group insurance contract, the larger the percentage of the group that can be included, the better will be the experience, and thus the lower the premium.

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To the Editor:—"Social In-Security—The Trap Awaiting the Young M.D." by Webster and Coffey in the Sept. 15 issue of The Journal, page 231, is a very interesting and provocative article. However, there are a couple of questions and circumstances the authors do not cover. For example, they omit mention of the credit allowed for military service. There are more than a few medical reservists who were called to active duty as much as 18 months before Pearl Harbor, served six years, and then another two during the Korean conflict. This equals eight years' maximum premiums under social security that the ex-service man receives gratis. Medical Economics, Inc., published a report of a survey of physicians in which the doctors, by a slight majority, did not favor compulsory social security legislation. However, among psychiatrists 64% favored the measure. More than 90% of psychiatrists are full-time or part-time government employees and, being "pension conscious," seek to supplement their retirement provisions. If ordinary insurance offers better and cheaper coverage, why have underwriters, accountants, economists, etc., not enlisted congressional support to repeal social security? Why did the legal profession become subscribers to social security only this year? Certainly somewhere there must be a shrewd attorney, particularly a tax expert, who could detect the same flaws and disadvantages as were picked up by Webster and Coffey.

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To the Editor:—Enclosed are two pamphlets on social security (Poirot, P. L.: *Social Security*, New York, the Foundation for Economic Education, Inc., 1954. Manion, C. E.: The Social Security Tax, reprinted from *Ideas on Liberty*, no. 3, November, 1955, New York, the Foundation for Economic Education, Inc.). I am forwarding them after seeing in The Journal the articles by Webster and Coffey entitled "Social In-Security—The Trap Awaiting the Young M.D." in the Sept. 15 and 22 issues, pages 231 and 426 respectively. They discuss thoroughly the economic aspects of social security. Would it not now be appropriate to point out some of the moral, constitutional, and basic Americanism aspects of this monstrosity? These two articles may be reprinted without the necessity of applying for permission, which, in any event, would be freely given and which could aid physicians in making up their minds on this matter.

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THE PHYSICIAN AND DISASTER

To the Editor:—Concerning the editorial "The Physician and Disaster" in the Nov. 3, 1956, issue of The Journal, page 977, I agree that local planning for disaster is the logical beginning. Coordination can then be achieved with state and region, rather than attempting to accomplish this from "above" or at national level. In Tulsa, Okla., each physician has a disaster assignment in the form of a certificate that he has received by mail, signed by the president of the county medical society and the civil defense medical director. Assignments were made for hospital duties, auxiliary hospital duties (in high schools), and field aid stations. There are no conflicting assignments. In this manner it is hoped that knowledge of a disaster situation will automatically cause each physician to proceed to his regular post of duty without undergoing the preliminary period of confusion that otherwise might ensue.

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WHIPLASH INJURY

To the Editor:—The article by Gotten, "Survey of One Hundred Cases of Whiplash Injury After Settlement of Litigation" (*J. A. M. A.* 162:865 [Oct. 27] 1956) is the best approach to the problem that I have yet read. However, it is based only upon cases that were the subject of litigation and the conclusions are of necessity *post hoc, ergo propter hoc*. The figures can have no valid meaning until someone makes the same study, using the same questionnaire on the same number of cases of whiplash injury that have not been the subject of litigation. I strongly suspect that in such a control study the percentage recovery, length of disability, symptoms, and permanent disability will not be much different in the two series. Gotten's description of the mechanism of whiplash injury follows the common error, stating that when the victim's car is struck "from behind or from the side. His body is suddenly thrust in a position of acute flexion, followed by extension of head." This is exactly the reverse of the fact. Abbott, in his comment on Gotten's article (*J. A. M. A.* 162:917 [Oct. 27] 1956), is to be complemented for a diagram showing the correct mechanism. It is also correctly shown on page 48 of the excellent monograph "The Cervical Syndrome" by Ruth Jackson (Springfield, Ill, Charles C Thomas, Publisher, 1956), which should be required reading for everyone interested in the subject. I would also recommend the "Symposium on Whiplash Injuries" in the *International Record of Medicine and General Practice Clinics* for January, 1956, pages 1 through 30.

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AMINOMETRADINE FOR TOXEMIA OF PREGNANCY

To the Editor:—I read with great interest the report of the Council on Pharmacy and Chemistry on aminometradine (Mictine) published on page 116 of the Sept. 8 issue of The Journal. Of particular interest to me was the sentence in the fourth paragraph, which reads as follows: "Sufficient valid evidence is lacking, however, of the drug's usefulness in toxemia of pregnancy or premenstrual tension." I have no quarrel about the usefulness of the drug in premenstrual tension, since I have had no experimental work to substantiate this claim. However, I would like to take exception to the statement about its usefulness in toxemia. My associates and I have carried out a substantial amount of research regarding the metabolic effects of aminometradine in toxemia of pregnancy. The first report of Voskian and myself was published in the July issue of the *Journal of Applied Physiology* (9:111, 1956). The data included in this paper show clearly that aminometradine produces a significant increase in water and electrolyte excretion, thereby improving the edema of both normal patients and patients with toxemia. No changes in the factors that control acid-base regulation were found. The effects of aminometradine were even more striking in patients with toxemia than in normally pregnant ones. At the present time, we are compiling the data obtained during the last two years from ambulatory pregnant patients who were given aminometradine for alternate periods Clinically and experimentally, the data indicate that aminometradine is an effective drug in toxemia and that the side-effects are minimal. Under these circumstances, it seems to me that the evidence toward its usefulness in toxemia is just as favorable as in cardiac or nephrotic edema.

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HEART CATHETERIZATION

To the Editor:—The 1956 Nobel Prize for Medicine was awarded to one German and two American physicians for catheterization of the heart. According to news releases the experiments of Forssmann, the German scientist, date back to 1929. In this connection it may be of interest that catheterization of the heart was performed in 1908 by Fritz Bleichroeder, chief resident of the medical department of the Municipal Hospital Gitschenerstrasse in Berlin, Germany. Bleichroeder was in no way interested in the physiology or pathology of the heart. He was interested in the carbohydrate metabolism and wanted to obtain blood from the heart after 125 gm. of glucose was ingested. After numerous experiments on dogs without any accident, he successfully catheterized the heart of Joseph Portmann, laboratory technician at the hospital. Bleichroeder's approach to the heart was from the femoral vein. The procedure was done with a ureteral catheter. At the time of Bleichroeder's experiments I was intern at his department. When I finished my internship, Bleichroeder's investigations were not yet finished. I then became a ship's surgeon of the Hamburg American Line, and I don't know whether the procedure was ever published.

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MISCELLANY

Following is a special report prepared by the Washington Office of the American Medical Association.—Ed.

FEDERAL MEDICAL-HEALTH SPENDING FOR FISCAL YEAR ENDING JUNE 30, 1957

This is our fourth annual report on the federal medical budget. To the extent we can make it so, it is a factual, objective study of how much the U. S. government is spending this fiscal year in all health and medical fields. We are dealing with money that has been appropriated and currently is available to be spent. This special report is based on the actual appropriations, and on information obtained directly from federal agencies and departments.

When talking in billions of dollars, it is often difficult to make the totals meaningful. However, here are some conclusions:

1. What the federal government is spending in health fields alone represents an average cost of $15.17 per man, woman, and child (Population, family-size, and employment figures from the census bureau). Incidentally, it is costing each of them $1.78 more this year than last.
2. If only wage-earners are considered, they will be paying on the average $38.72 each to finance the federal government's health-medical operations. That is $4.40 more than they paid last year.
3. The average family will be paying $54.61 this year for the U. S. government's health-medical activities.
4. Even in an over-all federal budget of 61.2 billion dollars, the total health cost is not insignificant. It is a billion dollars more than the cost of running the Commerce Department, half a billion more than all Agriculture Department expenses, and six times the Interior Department's budget.
5. Mostly because of spectacular increases for research, health programs of the Department of Health, Education, and Welfare this year will cost half again as much as they did last year.
6. For the first time since World War II, the medical costs of the Veterans Administration top the list, passing the Defense Department. A close third is the Department of Health, Education, and Welfare.

This report is based on spending alone. We do not undertake to evaluate the many individual programs. Obviously many of them are necessary just to maintain the United States' unsurpassed public health standards. Others undoubtedly will pay rich dividends in procedural and scientific discoveries. Some probably could be questioned. But the only purpose of this study is to show exactly what they cost.

MEDICAL-HEALTH BUDGETS OF FEDERAL DEPARTMENTS, AGENCIES, AND COMMISSIONS FOR THIS FISCAL YEAR

Summary of Budgets

Agency	Fiscal 1957	Fiscal 1956
Veterans Administration	$825,024,300	$790,185,800
Department of Defense	790,105,000	818,104,700
Department of Health, Education, and Welfare	772,661,800	526,935,400
Federal Civil Defense Administration	49,810,000	30,450,000
Atomic Energy Commission	31,525,000	27,700,000
International Cooperation Administration	29,310,000	25,441,000
Department of State	15,496,000	13,669,790
Federal Employees Health Program	10,000,000	6,000,000
National Science Foundation	8,000,000	5,000,000
Department of Labor	7,151,126	7,336,000
Department of Interior	6,138,205	5,770,000
Panama Canal Zone	6,055,300	5,702,900
Department of Treasury	3,511,700	2,900,000
Department of Justice	1,580,000	1,470,000
Federal Trade Commission	1,000,000	1,000,000
Department of Commerce	547,914	277,586
Civil Service Commission	386,000	382,600
National Advisory Committee to Selective Service	180,000	180,000
President's Committee for Handicapped	134,678	130,000
Health Resources Advisory Commission	90,000	101,000
Office of Attending Physician of Congress	12,145	......
Totals	$2,558,719,168	$2,268,826,576

VETERANS ADMINISTRATION
(This Year: $825,024,300—Last Year $790,185,800)

Inpatient Care in VA Hospitals..............................$619,614,000

(Last year: $615,869,000)

The VA's largest single medical appropriation covers inpatient care in 173 VA hospitals and provides for an average of 121,865 beds a day. At present the VA reports daily patient load at 111,540, just over 91% of capacity. The appropriation includes salaries of physicians and other personnel, medical rehabilitation of veterans, dietetic and nursing services, social services, and special services, such as recreation and transportation of veterans.

Outpatient Care $82,638,000

(Last year: $85,471,200)

The bulk of this appropriation is for outpatient care in about 100 VA clinics. The remainder is earmarked for fees to physicians ($7,738,000) and dentists ($8,415,000) under the home town care program.

Modernization and Replacement Construction........$51,635,000

(Last year: $30,000,000)

This amount is for work on existing units costing over $250,000 a project and equipment for new units. The money is available until expended. (See Major Alterations and Improvements item for smaller projects.)

Domiciliary Care $29,319,000

(Last year: $23,062,500)

Domiciliary care is being provided in 17 VA facilities for about 17,000 veterans who, while incapacitated for employment, are not in need of full hospital care. The VA also makes payments to 30 state homes in approximately 30 states with a daily patient load of around 9,000. Payments this fiscal year are estimated at $5,888,000 (under Public Law 613, 83rd Congress, federal contributions to these homes were raised from a maximum of $500 to $700 a year per patient).

Contract Hospitalization $13,967,000

(Last year: $15,237,300)

This appropriation finances an average daily patient load of 3,260 veterans in federal hospitals other than VA and in state and municipal hospitals. Patients in federal non-VA hospitals are estimated at 1,345 and in nonfederal hospitals, 1,915. Psychotic cases make up the largest single category of contract cases.

Medical Administration $7,300,000

(Last year: $7,422,000)

To operate the VA Department of Medicine and Surgery in the Washington central office and the seven area medical offices; included are salaries, travel, and like expenses.

Medical Research $10,990,300

(Last year: $ 6,381,600)

For research, mostly in VA hospitals. The breakdown: general medical and surgical research, $5,870,000; atomic medical research, $2,000,000; prosthetics testing, $990,300; neuropsychiatric, $1,250,000; tuberculosis, $780,000; and other, $100,000.

Major Alterations, Improvements, and Repairs..........$4,533,000

(Last year: $3,900,000)

For alterations, improvements and repairs to VA clinics and domiciliaries (costing less than $250,000 per project).

Supply Depot Operations..$1,628,000

(Last year: $1,642,200)

For maintaining and operating supply depots handling the purchase, shipping, and storage of medical supplies and equipment used by the Department of Medicine and Surgery.

Medical Education and Training...............................$1,400,000

(Last year: $1,200,000)

For VA training programs for physicians and other VA personnel, in medical specialties and auxiliary services.

Medical Care—Philippine Veterans...........................$2,000,000

(Last year: not reported)

Until 1960 the U. S. government will contribute for the care of Philippine veterans.

DEPARTMENT OF DEFENSE
(This Year: $790,105,000—Last Year: $818,104,500)

Army Medical Services*............................Approx. $290,000,000

(Last year: $300,000,000)

Air Force Medical Services*......................Approx. $223,000,000

(Last year: $286,000,000)

Naval Medical Services*...........................Approx. $277,000,000

(Last year: $232,000,000)

The estimated costs for the medical services of the Army, Air Force, and Navy include expenses normally associated with the operation of military hospitals and dispensaries, military and civilian salaries, medical supplies and equipment, utilities, communications, transportation, travel subsistence, maintenance and repair of buildings and grounds, expenses for construction, medical education and training, medical research, and preventive medicine.

Office, Assistant Secretary of Defense
(Health & Medical)....................................Approx. $105,000

(Last year: $104,500)

For salaries, travel and administration of this office, and for travel expenses and consultant fees for the Defense Department Civilian Health and Medical Advisory Council.

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
(This Year: $772,661,800—Last Year: $526,935,400)

Division of Hospital Facilities...............................$126,381,000

(Last year: $112,250,000)

This division administers the federal aspects of both the original and expanded Hill-Burton programs. The total appropriation is divided into the following four categories:

Hill-Burton Original Program...............................$102,800,000

(Last year: $ 88,800,000)

This appropriation, allotted to the states on the basis of population and per capita income, assists in the financing of new hospitals and related health facilities construction under the original Hill-Burton program. To date federal funds have partially financed approximately 2,869 projects, including nearly 132,096 hospital beds, and 636 public health centers, 18 state health laboratories and approximately 100 nurses homes and training facilities. To date federal contribution represents $762,000,000 and is matched by sponsors' funds amounting to $2,370,000,000.

Medical Facilities (Category Program)..................$21,000,000

(Last year: $21,000,000)

The total allotted to the states this year on a population-per capita income formula will assist in the financing of new construction under the 1954 amendments in four categories as follows: $6,500,000 for hospitals for the chronically ill and impaired; $6,500,000 for diagnostic centers, or diagnostic and treatment centers; $4,000,000 for nursing homes; and $4,000,000 for rehabilitation facilities. As under the original program, the federal share may range from one-third to two-thirds of the total project cost. As of July, 1956, there was approved a total of 204 projects divided among the four categories as follows: facilities for chronically ill, 42; diagnostic-treatment centers, 77; nursing homes, 42; and rehabilitation facilities, 43.

Hill-Burton Administrative Expenses.......................$1,381,000

(Last year: $1,250,000)

This appropriation is used for salaries and expenses for the hospital survey and construction program for Washington, D. C., and eight regional offices at the federal level.

Research $1,200,000

(Last year: $1,200,000)

Authorized in 1949 but not appropriated until 1955 was this item for research, experiments and demonstrations on utilization of hospital services, facilities, and resources. The bulk of the money is earmarked as grants to states, universities, hospitals, hospital associations, professional associations, and community organizations, and a small amount for direct research by the Public Health Service.

National Institutes of Health...................................$216,508,000

(Last year: $ 97,823,000

The total for the institutes is appropriated as follows:

National Cancer Institute..$48,432,000

(Last year: $24,828,00

About two-thirds of this appropriation is earmarked for gran to nonfederal individual investigators and private institutions f research and training and states receive $2,250,000 for canc control work. The balance is used for direct operations, salari supplies, and for this institute's share in the cost of operatin the Bethesda (Md.) Clinical Center and related auxiliary servic

National Heart Institute..$33,396,00

(Last year: $18,778,00

Grants to nonfederal individual investigators and public and private institutions for research and training take about two-thirds of the appropriation, and $2,125,000 is allocated to states for heart disease control. The remainder is for direct operations, such as salaries and supplies, and to support the Clinical Center.

Mental Health Institute...$35,197,000

(Last year: $18,001,000)

Approximately 60% of this appropriation is apportioned for research and training through grants to individual investigators and public and private institutions. The sum of $4,000,000 is allocated to the states for community mental health services. The remainder will support direct operations, such as salaries, expenses, and to help finance the Clinical Center and related auxiliary research services.

Arthritis and Metabolic Diseases Institute................$15,885,000

(Last year: $10,740,000)

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*All figures are estimates because appropriations are not broken down into categories of medical expenditures. Anticipated reduction in the Department of Defense medical program during fiscal year 1957 is primarily attributable to more effective joint utilization of the facilities, fewer personnel assigned to operation, and a lower level of hospital and dispensary construction. Reductions, however, have been partially offset by an estimated expenditure of 41 million dollars during fiscal year 1957 for the Dependent Medical Care Program.

Grants to public and private investigators for research and training total $10,290,000. The remainder will go for direct operations, such as salaries and supplies and Clinical Center support.

Neurological Diseases and Blindness Institute..........$18,650,000

(Last year: $ 9,861,000)

Grants to public and private investigators and institutions for research and training total $14,280,000. The remainder is for direct operations, such as salaries and supplies and to support the Clinical Center.

Allergy and Infectious Diseases Institute................$13,299,000

(Last year: $ 7,580,000)

Research grants to public and private investigators for research and training amount to $8,182,000. The remainder finances direct research and other related services of the Institute.

Dental Health Institute...$6,026,000

(Last year: $2,136,000)

This appropriation is divided as follows: (*a*) for research and fellowships, $3,700,000, (*b*) direct research at Bethesda, $1,035,000, (*c*) review and approval of research grants and fellowships, $79,000; (*d*) administration, $100,000; (*e*) technical assistance to states, $824,500; and (*f*) coordination and development of dental resources, $287,500.

National Institutes of Health—General Funds........$12,122,000

(Last year: $ 5,899,000)

These funds are administered by the Division of Research Grants of the National Institutes of Health, with practically all funds being expended for research and training grants, with the exception of 1.7 million dollars for control of biologics (including polio vaccine), which activity is under the Division of Biologics Standards. The balance goes toward supporting fellowships and administrative expenses relating to grants.

NIH Planning and Construction...............................$33,501,000

(New category)

There is available for NIH for planning or construction of facilities $33,501,000 broken down as follows: $1,630,000, expansion of surgical NIH units, $200,000, planning for future construction for dental NIH research; $1,371,000, for animal quarters, NIH, $300,000, planning for office building, NIH; $30,000,000 grants for medical research facilities under Public Law 835.

Indian Health Activities...$48,075,300

(Last year: $38,840,000)

Under Public Law 568 (83rd Congress) PHS assumed responsibility for health of American Indians and natives of Alaska, which formerly was a function of Interior Department. The total is broken down as follows: hospital care in Indian hospitals, $23,001,400, contract patient care, $8,313,000, field health services, $5,940,600, program direction and management services, $2,058,300, and construction of hospitals, clinics and quarters, $8,762,000. The total appropriated for Indian health activities is $48,075,300, to which is added reimbursable items from other government agencies totaling $538,300.

Hospitals and Medical Care.......................................$40,969,700

(Last year: $34,326,000)

These funds are used for operational cost and maintenance of PHS hospitals and health services in caring for American seamen, Coast Guard and Public Health Service personnel and their dependents, Federal employees injured at work, leprosy patients, and narcotic addicts; includes studies in the development and coordination of nursing resources. It also includes $1,000,000 for grants to Hawaii for care of patients suffering from leprosy and $2,000,000 for nurse training grants. Not shown is approximately $800,000 additional income from reimbursable items from other federal agencies.

Poliomyelitis Vaccine Program..................................$23,600,000

(Last year: $30,000,000)

Public Law 411 extended last year's $30,000,000 poliomyelitis vaccine program. Additional appropriated funds amounting to $23,600,000 are available in addition to unexpended appropriations of last year to states for vaccination of children under 20 and pregnant women against poliomyelitis. The federal vaccination program is scheduled to expire on June 30, 1957.

Assistance to States—General....................................$17,591,000

(Last year: $18,160,000)

Grants totaling $12,000,000 will be available for apportionment to the states in support of state and local general public health activities. These grants must be matched one state dollar for every two federal dollars. Last year $4,500,000 was available for activities in administering the polio vaccination programs in the states. An additional $4,591,000 supports direct activities of the U. S. Public Health Service in providing technical assistance, consulting services to states, expenses of the National Office of Vital Statistics, international health activities, demonstrations, training activities, and operational expenses. An additional $1,000,000 will be available for grants to schools or direct traineeship awards to individuals for the training of professional public health personnel. In this program matching will be required.

Tuberculosis Control $6,660,000

(Last year: $6,000,000)

Grants to states for diagnostic and treatment clinics, mass case-finding, and follow-up services account for $4,500,000, all of which has to be matched equally by the states. The remainder is for direct operations of PHS.

Communicable Disease Control..................................$5,750,000

(Last year: $5,250,000)

The entire appropriation is used for direct activity of the PHS Communicable Disease Center at Atlanta, Ga., and its affiliated operations, including investigations in poliomyelitis. The center carries on studies in epidemiology, furnishes laboratory diagnostic services and sponsors special projects to assist states.

Sanitary Engineering Activities...................................$9,000,000

(Last year: $4,690,000)

This program is made up of seven activities as follows: air pollution, $2,740,000; water supply and water pollution control, $4,224,100; radiological health activities, $347,800; milk and food sanitation activities, $446,000; interstate carrier and general sanitation activities, $493,000; Sanitary Engineering Center research activities, $403,100; accident prevention, $51,000; and administration, $295,000.

Venereal Disease Control...$4,195,000

(Last year: $3,500,000)

Of the total, $1,700,000 goes for direct grants to states for venereal disease detection, treatment and control on a special need basis. The remainder is spent for technical assistance to the states, mostly to pay federal employees assigned to state health departments.

Foreign Quarantine Service...$3,315,000

(Last year: $3,000,000)

This service operates approximately 250 medical quarantine stations on borders of the United States. It also operates approximately 25 medical examination stations on foreign soil for the examination of aliens seeking visas to enter the United States. Inspections are made of all seagoing vessels and aircraft entering the United States.

Office of the Surgeon General..............................$3,892,000

(Last year: $2,762,000)

For administrative expenses of this office, including all housekeeping services, evaluation of public health needs, and personnel training. Included also is $700,000 for administration of the National Health Survey Act authorized by Public Law 652.

Water Pollution Control..$50,000,000

(New category)

Under a new law passed by Congress in 1956 (Public Law 660), the federal government will make grants for waste treatment plants.

National Library of Medicine......................................$1,376,000

(New category)

As a result of Public Law 941 enacted by Congress in 1956, the Army Medical Library has been renamed the National Library of Medicine and transferred to the Department of Health, Education, and Welfare. While it is contemplated that a new structure will be erected to house the library, only operational funds and planning money have been made available by Congress for this fiscal year. Operational funds for the nine months which remained in the fiscal year following the transfer of the library to HEW total $1,026,000. An appropriation of $350,000 was made for planning the construction of a new library building.

Alaska–Disease and Sanitation Investigations
and Control $1,185,000

(Last year: $1,125,000)

This appropriation will be divided as follows: $638,000 for grants to the territory for public health services and the remainder for research activities of the Arctic Health Research Center at Anchorage.

Alaska Mental Health Program..$25,000

(New category)

Authorized by Public Law 830, which calls for the construction of a mental health hospital in Alaska and federal funds for operation of a mental health program. The first appropriation is for initial planning.

Reimbursable Health Program for Other
Governmental Agencies $321,800

(Last year: $321,800)

This represents the cost of services expected to be advanced by Public Health Service to other governmental agencies for establishing and operating on-the-job clinics. As a total, however, it is misleading, as a substantial number of government agencies carry on their own health programs independent of PHS. PHS deals largely with Washington personnel, whereas 90% of the government's employees are located outside of Washington.

Social Security Administration..............................$161,183,000

(Last year: $125,796,600)

The total includes:

Bureau of Public Assistance (medical
payments) ....Approx. $100,000,000

(Last year: $ 90,000,000)

An estimated $265,000,000 of federal, state and local funds is expected to be paid for medical and health needs of public assistance recipients this fiscal year. The United States' share of this total is an estimated $100,000,000. This bureau operates under the Social Security Administration.

Disability Freeze Program ....Approx. $9,000,000

(New category)

Among the administrative expenses of the Old Age and Survivors Insurance program, is an item incurred by excusing disabled persons from paying OASI contributions without penalty in their retirement payments. This phase of the program is referred to as the "disability freeze" amendment to the Social Security Act. This year approximately $9,000,000 will be expended for employees' salaries, working materials, etc.

Permanent and Total Disability Payments..Approx. $11,000,000

(New category)

Under the 1956 amendments to the Social Security Act, persons over age 50 who become permanently and totally disabled may receive payments equal to retirement benefits as though they had reached age 65. This new program will take effect on July 1, 1957. This fiscal year, however, expenses will be incurred for "tooling up." These expenses will include recruiting of additional staff for field offices, training of staff, revising manual materials, negotiation of new agreements with state agencies for rehabilitation, and the furnishing of new materials for states to use, such as forms, etc.

Children's Bureau $41,183,000

(Last year: $35,796,600)

Operating under the Social Security Administration, the Children's Bureau administers grants to states for maternal and child health, and crippled children's and child welfare services. This year grant money totals $39,361,000, divided as follows: $16,000,000 for maternal and child health work, with the states required to spend approximately 50 cents for each federal dollar, $15,000,000 for crippled children's services, same matching requirement; and $8,361,000 for child welfare services, where the only matching requirement is that states must supply some money. In addition the Children's Bureau has $1,822,000 to finance investigating and reporting activities and to administer the grants.

Food and Drug Administration.....................................$7,979,000

(Last year: $6,266,000)

For administering the federal Food, Drug, and Cosmetic Act, Congress voted $6,779,000, which includes $309,000 for policing the distribution of Salk poliomyelitis vaccine during this fiscal year. FDA will also realize an estimated $1,200,000 from fees paid by industry for certification of biologics, insulin, seafood, etc. The figure for last year does not include fees

Office of Vocational Rehabilitation............................$42,110,000

(Last year: $36,825,000)

Under the expanded Vocational Rehabilitation Act (Public Law 565, 83rd Congress) Congress this year voted $36,000,000 for grants to states. This is divided as follows: (a) support of basic rehabilitation services including medical examination, surgical and therapeutic treatment, hospitalization, prostheses, occupational tools and aids, vending stands, rehabilitation facilities, vocational training, and funds for maintenance (based on per capita income and populations as in Hill-Burton), $33,500,000; (b) extension and improvement of state programs, $1,500,000; (c) special grants to states or nonprofit organizations for projects designed to expand the rehabilitation program (2-1 federal-state matching), $1,000,000. In addition $2,950,000 is available for training of rehabilitation personnel, including physicians, therapists, psychologists, counselors, medical, and psychiatric social workers; $2,000,000 for grants to states and other public and nonprofit agencies and organizations to pay part of the cost of special research and demonstration projects in vocational rehabilitation; and $1,160,000 for federal administrative costs.

United States Office of Education.............. Approx. $2,545,000

(Last year: not reported)

Practical Nurse Training: For a goodly number of years the Office of Education has been making grants to states for vocational education in all fields of endeavor. It is estimated that during the last fiscal year approximately $500,000 in grants was used to educate practical nurses. For this year, the Office of Education has available $31,267,000 for grants to states. Included in this figure is $2,000,000 earmarked funds recently authorized by Congress (practical nurses). An appropriation was voted in this amount, plus an additional $45,000 for added costs of administration. Office of Education officials believe that the states will not diminish the level of last year's program, which would mean approximately $2,545,000 is available for practical nurse education.

FEDERAL CIVIL DEFENSE ADMINISTRATION

(This Year: $49,810,000—Last Year: $30,450,000)

Projected health and medical spending by FCDA this year moves close to the $50,000,000 mark for the first time. Out of a total appropriation of $93,560,000, the estimated $49,810,000 spending for the FCDA health office includes $47,000,000 for stockpiling medical and other supplies owned wholly by the federal government, $1,700,000 for matching funds to the states to help them in their medical stockpiling, $810,000 for research, and $300,000 for administration costs.

ATOMIC ENERGY COMMISSION

(This Year: $31,525,000—Last Year: $27,700,000)

The Atomic Energy Commission's Division of Biology and Medicine has about 2.7 million dollars more than last year for research projects. This year's total includes the following spending plans: cancer, $3,002,000; other medical, $9,729,000; biological, $10,821,000; biophysical, $3,459,000; development of new laboratory equipment, $2,319,000; vocational and special training, $615,000; radioisotope distribution, $510,000; and miscellaneous items, $1,070,000.

INTERNATIONAL COOPERATION ADMINISTRATION

(This Year: $29,310,000—Last Year: $25,441,000)

Technical Cooperation Programs....$16,380,000

(Last year: $20,141,000)

The International Cooperation Administration through direct contributions (which do not have to be matched dollar for dollar) is helping underdeveloped countries to control specific diseases, to set up national and local health services and to establish environmental sanitation. Countries receiving money make contributions in cash, facilities or services in varying degrees.

Development Assistance Programs....$12,930,000

(Last year: $ 5,300,000)

Spending for emergency health programs (particularly in malaria control on which there is new world-wide emphasis) under ICA direction is up from last year. The agency has $2,500,000 for the Far East, and $10,430,000 for the Near East, South Asia, and Africa. The largest single beneficiary will be India.

DEPARTMENT OF STATE

(This Year: $15,496,000—Last Year: $13,669,790)

United Nations Children's Fund....$9,700,000

(Last year: $9,000,000)

The United States' share of the Children's Fund is up about $700,000 over last year for a total of $9,700,000, but the percentage of the United States' contribution to the total fund has dropped slightly from 60 to 57.5. This is due to the fact that some of the 65 other nations contributing have increased their share slightly. The fund is aiding about 264 health and medical projects in 92 countries and territories, benefiting 32 million children and mothers. Last year the fund treated 1,800,000 children for yaws, vaccinated 14,500,000 against tuberculosis, and 9,000,000 against malaria and other insect-borne diseases.

World Health Organization....$3,410,000

(Last year: $3,349,790)

The United States' share of the WHO budget remains at one-third of the total of all member nation contributions. Among the 84 countries agreeing to make contributions is Russia, which until recently has been inactive. Last year WHO was sponsoring about 500 health projects in 106 countries and territories. WHO's over-all budget is broken down this way: approximately 72% for operating programs, 10% for administration and salaries, and the rest for such expenses as holding international conferences, and to compensate for nonpayment by inactive member countries.

Pan American Sanitary Bureau....$1,386,000

(Last year: $1,320,000)

The United States is contributing approximately two-thirds of the bureau's regular budget which this year totals $2,100,000. In addition, the United States plans an extra $1,500,000 for 1957 malaria eradication programs. Because these international groups operate on a calendar year, the special contribution is not shown in this report. The bureau, in existence many years before WHO was organized, is the regional office of WHO for the Americas. The bureau is sponsoring health programs in 21 Latin American countries and the United States.

Foreign Service Employees Medical Care....$1,000,000

(New category)

The 84th Congress, under Public Law 828, broadened an existing medical care program for foreign service employees to take in their dependents, provided they are living overseas. State Department, which estimates that about 15,000 dependents are involved, has earmarked $400,000 for the first year. The regular program for overseas employees is placed at $600,000. Most of the care is provided in United States military facilities.

FEDERAL EMPLOYEES HEALTH PROGRAM

(This Year: approx. $10,000,000—Last Year: approx. $6,000,000)

Another health program, this one available to all federal civilian workers, provides limited services through health clinics. They are operated by federal agencies that employ 300 or more persons in any one area. By regulation, maximum cost of a health service cannot exceed $11 a year per employee, although special industrial conditions or minimal size unit may warrant a higher ceiling. Services include treatment for on-the-job illnesses and physical examinations for employment.

NATIONAL SCIENCE FOUNDATION

(This Year: $8,000,000—Last Year: $5,000,000)

The foundation's over-all budget of $40,000,000 is two and a half times last year's appropriation. While money earmarked for research grants in biological and medical sciences this year does not show the same proportionate increase, it is still considerably above the fiscal year 1956. The foundation, now in its sixth year, initiates and supports basic scientific research, evaluates research of government agencies, and correlates research programs of various agencies.

DEPARTMENT OF LABOR

(This Year: $7,151,126—Last Year: $7,336,000)

Bureau of Employees' Compensation....$6,600,000

(Last year: $6,800,000)

An estimated 2,390,000 federal workers now are eligible under the Federal Employees' Compensation Act for medical and hospital care, rehabilitation services, disability and death payments, and funeral and burial expenses. For treatment of employees by private doctors and hospitalization in private facilities, Labor Department has set aside $4,500,000 this fiscal year, and for similar services in federal hospitals and clinics, $2,100,000. A slight shift is noted away from federal facilities to private resources; last year's totals were $4,349,218 and $2,234,222.

Bureau of Labor Standards....$551,126

(Last year: $536,000)

For promotion of industrial safety, the bureau plans to spend $387,322, and for reemployment programs of the physically handicapped, $163,804. The agency develops standards for hazardous occupations, assists the states in accident prevention programs and trains personnel for administering various projects.

The detection of carcinoma in patients with achalasia is particularly difficult in view of the fact that dysphagia has usually existed for some time and does not increase with the development of malignancy. One of the most characteristic signs is the presence of anemia and hematemesis. Another sign was a foul odor to the breath caused by necrosis of the tumor.

Chronic irritation is generally considered to be a factor in the production of malignancy. This irritation in the esophagus may be the result of chronic ulceration secondary to lye burns or peptic esophagitis associated with hiatal hernia, or it may be bacterial as a result of stasis and infection in patients with achalasia of the esophagus and diverticulum. Though malignancy does not develop in many patients with each of these conditions, it is unwise to allow any of these conditions to persist untreated when complicated by a significant esophagitis. The existence of this complication must be acknowledged, the proper examinations frequently made, and the indicated therapy provided to eliminate chronic esophagitis in order to prevent later malignancy. No examination is complete without examining the esophagus by x-ray (only after proper cleansing) and by the esophagoscope, with the help of which the mucous membrane may be directly visualized.

Kaliopenic Nephropathy. J. W. Conn and R. D. Johnson. Am. J. Clin. Nutrition 4:523-528 (Sept.-Oct.) 1956 [New York].

Conn and Johnson collect the available evidence that chronic hypokalemia, always associated with a significant deficit of body potassium (kaliopenia), results in characteristic anatomic and functional lesions of the renal tubules. This lesion exists in the newly described clinical syndrome called primary aldosteronism. Since in the latter condition chronic hypokalemia occurs in man via a mechanism that is unique and that differs from previously recognized causes of potassium depletion, demonstration of the typical pathological and functional lesions of the renal tubules seems to relate this condition to lack of the potassium ion. Kaliopenic nephropathy must be recognized as a clinical and pathological entity. It can be induced experimentally by diets deficient in potassium. It is reproducible by repeated administration of large doses of desoxycorticosterone and is preventable when supplementary potassium is given in such experiments with desoxycorticosterone. In man, the syndrome is observed most frequently in the potassium-deficient state associated with chronic intestinal disease. It is also present in primary aldosteronism, the renal manifestations of which are analogous to desoxycorticosterone-induced "diabetes insipidus" in animals. A decreased tubular capacity to reabsorb water, not influenced by administered pitressin, is the most distinctive functional abnormality encountered in kaliopenic nephropathy. While other renal functions, too, may be impaired, hyposthenuria is disproportionately severe. Histologically, the lesion is limited to tubular cells and is characterized by diffuse hydropic vacuolarization. This anatomic lesion is observed in chronic hypokalemia in man no matter whether it is produced by long-standing diarrhea or by an aldosterone-secreting cortical tumor. In most instances both the functional and anatomic abnormalities appear to be slowly reparable after replacement of the potassium deficit. It is likely, however, that in some cases so much damage has occurred during chronic kaliopenia that functional recovery is impossible.

Nutrition in Chronic Renal Failure. A. J. Merrill. Am. J. Clin. Nutrition 4:497-508 (Sept.-Oct.) 1956 [New York].

The management of nutrition in chronic renal failure differs from that in acute renal failure in several respects: 1. The duration of the disease requires that the diet be adequate in caloric, vitamin, mineral, and protein content and that it contain proper amounts of the essential amino acids. 2. The diet must be palatable, since tube feeding is impractical and undesirable for extended periods and because a tasty diet is essential to the morale of these patients whose appetite at best may be none too good. 3. Potassium intoxication is not so common as in acute renal failure, since the urine volume is usually ample except when the patient is moribund. 4. Fluid control is not so exacting as in acute renal failure, because the urine volume can adapt itself to the intake of fluids within variable limits. Chronic renal failure affecting chiefly the glomeruli produces problems of abnormal retention of substances, whereas chronic tubular disease produces deficits principally of cations. The latter is simpler to treat, although there is a lack of adaptability to either deficits or excesses.

Water intake should be high unless water retention or edema is present. Forcing fluids in the presence of edema will cause deterioration of renal function. The salt intake should average about 4 or 5 gm. daily; it should be reduced with water retention, but few patients will tolerate rigid restriction. Massive amounts of salt may be required in unusual instances. Potassium abnormalities are treated as indicated by the blood level and excretion studies. Patients with plasma potassium levels above 5.5 Meq per liter should be either watched very carefully or treated with a potassium-absorbing resin. Calcium deficiency without blood phosphorus elevation responds well to oral administration of calcium, vitamin D, and alkali administration (after milk-alkali administration, vitamin D intoxication, and hyperparathyroidism have been ruled out). If the blood phosphorus is high, these measures are futile and phosphorus has to be eliminated with aluminum hydroxide. The diet should contain about 0.5 gm. per kilogram of body weight of animal protein daily, supplied by a protein of high biological value, about 3 to 4 gm. per kilogram of carbohydrate and 1 to 1.5 gm. per kilogram of fat. In an addendum to this report the author presents a menu for a diet containing approximately 2,200 calories, 50 gm. of protein, and 4 gm. of salt.

SURGERY

Five-Year Postoperative Results of First 500 Patients with Blalock-Taussig Anastomosis for Pulmonary Stenosis or Atresia. B. D. White, D. G. McNamara, S. R. Bauersfeld and H. B. Taussig. Circulation 14:512-519 (Oct.) 1956 [New York].

Three hundred eighty-nine of the first 500 patients with a Blalock-Taussig anastomosis for pulmonary stenosis or atresia survived six months or longer after the operation. Sixty-seven of the 389 patients were lost to follow-up. Eleven patients who survived the operation were unimproved by their first operation. In an additional 67 patients a five-year follow-up was not completed at the time the authors' study was closed. Thus there remain 244 patients originally improved by a Blalock-Taussig anastomosis who have been followed up for five years or longer, of these, 226 obtained good results, i. e., their exercise tolerance was virtually normal and their hearts were stationary in size, with a cardiothoracic ratio of 60% or less. The hemograms were also stationary, with a maximum red blood cell count of 6,500,000, a maximum hemoglobin of 17 gm., and a maximum hematocrit reading of 55 volumes per 100 cc. Eighteen obtained fair results from the first anastomosis. The good results were maintained in 163 patients (67%) five to eight years after the operation, and in 16 patients (7%) the results were still fair after the lapse of time. Nine patients (4%) were no longer improved and 23, i. e., 9% of those originally improved, required and survived a second operation.

Thirty-three patients (14%) died between six months and eight years after the operation. A higher percentage of patients with tetralogy of Fallot maintained good results postoperatively than of those with other malformations of the heart, and the mortality rate was significantly lower in the former group. One hundred twenty-six of the 163 patients with good results who were evaluated for changes in cardiac size, changes in the hemogram, and, whenever possible, changes in the arterial oxygen saturation, were in excellent condition in all respects. Twenty-three of the 163 patients had considerable nonprogressive cardiac enlargement. Fourteen patients had moderate and nonprogressive polycythemia. In most of these patients a good continuous murmur, which indicates that some blood is flowing from the aorta to the lungs, was observed. The best results were obtained in children who were between the ages of 8 and 12 years at the time of the operation. Subacute bacterial endocarditis was diagnosed in 15 (6%) of the 244 patients in the late postoperative period. Twenty-three of the 226 patients who originally obtained good results died, a late mortality rate of 11%, whereas 8 (44%) of the 18 patients who had obtained only fair results died. Of the 33 patients who died, 19 were no longer improved, 6 were losing ground, and 8 were doing well at the time of death. No patients with a tetralogy of Fallot died of cardiac failure.

These findings suggest that the optimum age for operation is between 8 and 12 years; 80% of the patients in this age group maintained their improvement five to eight years after the operation. The risk of postoperative subacute bacterial endocarditis, although real, is not great. Patients in whom the red blood cell count remains below 6,500,000, the hemoglobin below 17 gm., and the hematocrit below 55 per 100 cc. have an excellent long-term prognosis. A patient with these findings who has a tetralogy of Fallot and a cardiothoracic ratio of 50% or less has a particularly favorable prognosis.

Arterial Disease as a Cause of Pain in the Buttock and Thigh. G. Bonney. J. Bone & Joint Surg. 38-B:686-691 (Aug.) 1956 [London, England].

When a patient attends an orthopedic clinic with the complaint of pain affecting the calf of the leg, the possibility of arterial disease as a cause of the pain is usually remembered, but, when the pain is in the buttock or thigh, that possibility is often overlooked. Ten patients are reported on in whom pain due to arterial obstruction simulated pain caused by bone or joint disease or by disorder of the intervertebral disk. All patients had been considered to be suffering from conditions such as osteoarthritis of the hip or lumbosacral disk degeneration and had received treatment accordingly. Mistakes in the diagnosis may not only lead to mistaken treatment but may also cause delay in giving correct treatment and may lessen the chances of success. The pain differs only in site, not in character, from that affecting the calf in classic intermittent claudication. Palpable tibial pulses do not exclude a diagnosis of vascular insufficiency in the lower limb. In three of the patients claudication was present with palpable tibial pulse. In all of these the tibial pulse became impalpable after exercise to the point of pain. Ischemic changes in the peripheral parts of the limb are not necessarily a feature in these cases of proximal arterial obstruction. Only 1 of the 10 patients had marked peripheral ischemic changes. Radiography, by showing calcification in the site of the great vessels, is often a useful pointer to the diagnosis. It is suggested that in orthopedic clinics, where attention is often directed largely to skeletal abnormalities seen on radiographs of the lumbar spine, closer search for evidence of aortic or iliac calcification might be rewarding. Aortography was performed in most of the 10 patients and revealed occlusion either at the aortic bifurcation or of the iliac vessels.

Cancer of the Breast, 1661 Patients: I. Considerations in Future Therapy. R. C. Hickey, H. D. Kerr, R. T. Tidrick, and others. A. M. A. Arch. Surg. 73:654-660 (Oct.) 1956 [Chicago].

This series of 1,661 patients with breast carcinoma represented the recorded patient material for 24 years at the University Hospitals, State University of Iowa. The standard therapy for breast cancer was radical mastectomy, which was employed in 913 operable cases. Supplemental roentgen therapy was given in some of these cases. At five years from diagnosis, the over-all survival rate among the 1,661 patients was 36.8%. The five-year survival rate among all the patients treated by radical mastectomy was 46.8%. The five-year survival rate was 68.7% when the axillary nodes were free of cancer at the time of operation and 33.1% when they showed involvement. Roentgen therapy offered no measurable benefit in terms of survival and pattern of first recurrence; in general, these cases were clinically more unfavorable. Recurrence was most frequent locally and in the axilla. Local recurrence is discouraging, because this area is presumably cleared by radical mastectomy. Even when recurrence was delayed for 10 years, it was frequently local. The author feels that this reflects the biological characteristic of breast cancer rather than poor surgery. Furthermore, the first appearance of a distant metastasis was unpredictable, in that it sometimes occurred early even in patients in whom the cancer was presumably limited to the breast. The classic radical mastectomy should not be abandoned as yet. Techniques should be improved, and patients to be treated by radical mastectomy should be selected more carefully. Superradical surgery should be considered as a clinical experiment. It is hoped that public education to facilitate early diagnosis and prompt surgical treatment will lead to better results.

Comparison of Radical and Less Extensive Surgery in Cancer of the Breast. W. C. White. Am. Surgeon 22:942-947 (Oct.) 1956 [Baltimore].

The author prefers radical mastectomy, which he performed in 290 patients, to less extensive surgery in cancer of the breast. There were three surgical deaths. Of 134 patients without axillary metastases, 107 or 80% were alive after five years, whereas, of 153 with axillary metastases, 48 or 31% were still alive after five years. The over-all five-year survival rate was 53%. Radical mastectomy had been accepted for many years as an excellent procedure, but some surgeons believe that the Halsted procedure is not extensive enough, while others maintain that it is needlessly extensive, and even harmful. Superradical surgery involves greater operative risk than the other methods, and is not based on a clear-cut anatomic and pathological consideration. McWhirter advocates simple mastectomy followed by sterilizing roentgen irradiation of the regional lymph nodes. With this treatment he obtained a crude five-year survival rate of 58%.

In spite of the apparently similar survival rates in his own and McWhirter's case material, the author still believes that the radical Halsted procedure is preferable to McWhirter's method, although he feels that there is need for improvement in the treatment of patients with axillary metastases. In addition to surgery, aid for these patients may take the form of x-ray therapy, hormonal gland excision, testosterone therapy, or perhaps one of the new chemical compounds.

Preservation of Rectum in Familial Polyposis of the Colon and Rectum. S. T. Coleman and C. Eckert. A. M. A. Arch. Surg. 73:635-644 (Oct.) 1956 [Chicago].

Thirteen patients with polyposis of the colon are presented. Several of the patients were related to one another and others had blood relatives with polyposis of the colon and rectum. Familial polyposis is usually progressive. New polyps form, and in any one of them cancer may evolve. Total colectomy with proctectomy is the only means of freeing the patient from the risk of cancer. A single surgical procedure cannot meet the requirements in all patients, because of the different clinical situations encountered and the difficulty of predicting the rate of progression.

The authors have continued to employ total colectomy and ileoproctostomy and thereafter to control any polyps that may form subsequently within the rectum by endoscopic removal and fulguration. Ileoproctostomy may be employed when there are no polyps within the rectum or their numbers are small, that is, when the greater part of the rectal mucosa is normal. Cancer of the rectum, large sessile polyps, or total involvement of the mucous membrane of the rectum are obvious contraindications to the preservation of the rectum. If ileoproctostomy is to be done, there must be assurance of cooperation on the part of the patient if the rectum is to be preserved in familial polyposis, because regular follow-up examinations must be carried out, with prompt removal of polyps as they appear. If the surgeon is doubtful about the patient's cooperation, preservation of the rectum should not be considered. There were no surgical deaths in the 13 patients, but one patient had intraperitoneal abscesses, and mechanical intestinal obstruction developed in 2 others. Intestinal function is excellent in 12 patients, but one patient has involuntary stools at night. Colectomy does not appear to retard growth or physical development when carried out in childhood.

NEUROLOGY & PSYCHIATRY

The Treatment of Tuberculous Meningitis. H. V. Smith and R. L. Vollum. Tubercle 37:301-320 (Oct.) 1956 [London, England].

Two hundred thirty consecutive unselected cases of tuberculous meningitis were treated at Oxford and observed for at least one year. The first 80 patients were treated with streptomycin alone, and the survival rate was 52%. The next 70 patients also received streptomycin, but in addition certain patients were treated with intrathecal injections of the purified protein derivalast 80 patients received intrathecal injections of purified protein derivative of tuberculin routinely, except when some special contraindication was present, and the survival rate rose to 75%. The use of purified protein derivative of tuberculin is potentially dangerous, as it must be given in sufficient doses to provoke a reaction, which consists in an abrupt though temporary worsening of the meningitis. The patient is pale and drowsy; he vomits and, if sufficiently conscious, complains of headache and pain in the back. The temperature and intracranial pressure, rise while the physical signs and mental changes become more marked. This clinical disturbance usually begins 8 to 12 hours after the injection of purified protein derivative of tuberculin and lasts 12 to 36 hours. The clinical disturbance is the price that must be paid for the meningeal reaction. Early in treatment the intensity of the clinical component tends to outstrip that of the cerebrospinal fluid component, but after a few reactions this relationship is reversed and brisk cerebrospinal fluid reactions can then be obtained at the cost of only a mild and transient clinical upset.

Measures designed to minimize the danger of the reaction are discussed. Cortisone has proved lifesaving in a few carefully selected cases. As, however, it is in many respects antagonistic to tuberculin, it has seldom been used with this treatment. It is concluded that intrathecal medication is still required for the optimal treatment of tuberculous meningitis; that purified protein derivative of tuberculin is a useful adjuvant to the chemotherapy; that these cases are best treated at special centers; and that, if the very advanced cases could be eliminated by earlier and more accurate diagnosis, recovery could be expected in approximately 100% of cases.

Pheochromocytoma and Electroconvulsive Therapy. F. R. Drake and F. G. Ebaugh. Am. J. Psychiat. 113:295-301 (Oct.) 1956 [Baltimore].

The authors present the history of a 34-year-old woman who died from cardiac arrest following electroconvulsive therapy. Autopsy revealed pheochromocytoma of the left adrenal. The case is presented so that other psychiatrists may become more aware of a tumor that can produce symptoms similar to those found in various anxiety states with or without depression. The diagnosis was particularly difficult, as no paroxysm of hypertension was ever detected. In addition, there was no sustained hypertension to arouse suspicion. Although a little atypical, the patient's signs and symptoms suggested a tension depression. Pheochromocytoma is an absolute contraindication to electroconvulsive therapy.

Tight Filum Terminale. P. H. Jones and J. G. Love. A. M. A. Arch. of Surg. 73:556-566 (Oct.) 1956 [Chicago].

A review of the records of 442 patients with spina bifida occulta seen at the Mayo Clinic in the past decade disclosed 6 with tight filum terminale. The histories of these patients, of whom four were children from 3 to 12 years of age and two were adults aged 35 and 34 years, are presented. Most of them had sphincteric and locomotive difficulties that began in childhood and were progressive. Difficulty with micturition was common. Three of the four children and one of the adults had enuresis or urgency of micturition, or both. The urinary difficulties of one patient were worse in the morning. Another child had retention with overflow; improvement occurred after severance of a taut filum terminale. All six patients had locomotive difficulties. One girl had to stop attendance at ballet classes because of increasing inability to perform fine movements. One woman walked with a limp of the right leg. Another had noted weakness and atrophy of the left leg since the age of 4 years. By the time she reached high school age, the weakness had increased and pain had appeared in the same leg. In the ensuing years, weakness progressed and numbness commenced. The pain was aggravated by coughing and sneezing. There was limping and stumbling when walking. One girl complained of difficulty in using the left leg and stiffness of the knees. A boy had clawing of the toes of the right foot and stiffness of the knees during the two years before admission.

Stigmas of spina bifida were present in five patients. Increased quantities of hair were noted in three, a fat pad in two, and a fovea sacralis in another. A meningocele was present in one child. Roentgenograms of the lumbar spine revealed spina bifida in each patient. A tight filum terminale must be differentiated from other congenital anomalies and tumors and degenerative and inflammatory diseases. When progression of symptoms is seemingly from childhood and is accentuated at puberty, an anchoring of the spinal cord by a tight filum terminale is a strong possibility, and any patient with symptoms and signs of a progressive lesion should be subjected to surgical exploration. In each of the six patients presented, an intradural lumbosacral exploration was made and the tight filum terminale was resected. The results of the operations were gratifying. Recovery seemed commensurate with the severity of the preoperative symptoms and signs.

Carbohydrate Metabolism and Nutritional State in Multiple Sclerosis. H. Droller and I. J. N. Powell. J. Chron. Dis. 4:283-291 (Sept.) 1956 [St. Louis].

Observations in the course of glucose tolerance tests and on pyruvic acid levels had suggested that a disturbance of the carbohydrate metabolism played a part in multiple sclerosis. The pyruvic acid levels were considered particularly important because they implied a thiamine deficiency. The diphosphate of thiamine (cocarboxylase) is required for the decarboxylation of pyruvate, and, in its absence, glucose oxidation stops at the pyruvic acid level. Pyruvate then accumulates in tissues and blood. An investigation was undertaken into the nutrition and carbohydrate metabolism of 10 patients with multiple sclerosis who subsisted on diets of their own choice. There were five men and five women. The general level of nutrition was poor, the intake of fat and protein was low in both sexes, and the carbohydrate intake was low in women. The thiamine and niacin of the diet appeared adequate. The observed patterns of abnormal glucose tolerance tests corresponded to those seen in starvation and could be rectified by glucose feeding. Diabetes was discovered in one of the patients after glucose feeding. There was no biochemical evidence of thiamine deficiency in these patients subsisting on poor diets, but temporary thiamine deficiency developed in one patient after extra loading with glucose. Glucose tolerance curves, following the administration of thiamine and cocarboxylase, respectively, were of similar pattern. Cocarboxylase and thiamine had no therapeutic value.

GYNECOLOGY & OBSTETRICS

Corticotropin in Severe Infections and in Postoperative Disease in Gynecology. P. Alfieri. Minerva ginec. 8:387-392 (May 15) 1956 (In Italian) [Turin, Italy].

Three patients with peritonitis, one with postembolic pneumonia, and two with postoperative syndrome were treated with small doses of corticotropin, 10 mg. every six to eight hours. Treatment lasted for from three to five days. The results were good and in some cases they were very good. There were no untoward side-effects. Antibiotics and vitamin C were combined with the hormonal treatment.

Ulcerative Colitis and Pregnancy. I. Macdougall. Lancet 2:641-643 (Sept. 29) 1956 [London, England].

This report concerns 100 pregnancies in 64 women among 398 patients (244 women and 154 men) with ulcerative colitis who attended the Gordon Hospital in eight years ending June 30, 1955. The ulcerative colitis began during or immediately after the pregnancy in 26 of the 64 women. A high proportion of these women had a severe form of ulcerative colitis. A quarter of all women with ulcerative colitis who had been pregnant had their first attack during either pregnancy or the puerperium. Inactive colitis was unaffected by pregnancy. Active colitis was improved in one-half, unaffected in a quarter, and aggravated in a quarter of the pregnancies. The proportion relapsing rises to a third when the puerperium is included in the time of onset of the ulcerative colitis. Successive pregnancies do not have a consistent effect on ulcerative colitis. The Ulcerative colitis does not adversely affect pregnancy. The most interesting feature of the behavior of ulcerative colitis complicated by pregnancy is the high proportion of women who experience a remission. In this a parallel could be drawn with rheumatoid arthritis, which responds to pregnancy in the same way. The link may be hormonal, for there is strong evidence that a large percentage of patients with ulcerative colitis give a good clinical response to treatment with either cortisone or corticotropin, and this is rather like the way the condition reacts to pregnancy.

The "Fern Test" of the Cervical Mucus as a Pregnancy Test. K. J. H. Verschoof. Nederl. tijdschr. geneesk. 100:2578-2583 (Sept. 8) 1956 (In Dutch) [Haarlem, Netherlands].

The formation of crystals in the dried mucus of the cervix uteri was first pointed out by Papanicolaou in 1946. The crystals appear in a palm-leaf or fern-leaf pattern during the follicular phase of the menstrual cycle, when the cervical mucus is watery, light, and transparent. The test has been variously designated as the crystallization, arborization, fern-leaf, or palm-leaf reaction of the cervical mucus. The uterine cervix, like the endometrium, undergoes cyclical changes. During the follicular phase (from the 5th to the 22nd day) of the cycle, under the influence of estrogenic substances, crystallization is evident in the dried cervical mucus, but after the corpus luteum forms, and the formation of progesterone becomes dominant, crystallization (fern-leaf) formation is inhibited and the fern test becomes negative. Now the dried mucus shows cells only and is devoid of crystals. The same is true during pregnancy, the dried mucus is cellular, showing no crystals. If crystals in fern-leaf arrangement are found in the cervical mucus, there is no pregnancy. Several case histories are presented that illustrate the value of the fern-leaf pregnancy test.

Transplacental Passage of Vitamins A, E, and D_2 Injected Intravenously in the Mother. R. Decio and V. Alamanni. Minerva ginec. 8:381-387 (May 15) 1956 (In Italian) [Turin, Italy].

Water-soluble preparations of vitamins A, E, and D_2 were administered intravenously to pregnant women. The quantities present in the blood of the mother and of the fetus were then measured. The values of vitamin A that passed into the fetus were of from 50 to 62.5%, the values of vitamin E were of from 88 to 100%. Values were of from 45 to 47% and of from 20 to 23% respectively when the two vitamins were given intramuscularly. The passage of vitamin D into the fetus could not be measured exactly; however, the authors advanced the hypothesis that it could reach values of 100%.

PEDIATRICS

Miliary and Meningeal Tuberculosis: Difficulties in Diagnosis. R. S. Illingworth. Lancet 2:646-649 (Sept. 29) 1956 [London, England].

Illingworth fears that the decline in the incidence of miliary and meningeal tuberculosis may lead to a lessened awareness of these conditions as possible causes of a child's illness. The early diagnosis of tuberculous meningitis is vital; for with early treatment one can guarantee a recovery rate of over 90% without sequelae, whereas, if the treatment is delayed until the child is unconscious, the risk of death or of serious consequences is greatly increased. The author describes some of the diagnostic difficulties in 236 cases under his care in the Children's Hospital, Sheffield. One hundred ninety-two of these children were admitted with meningitis and 43 with miliary tuberculosis (of whom 13 developed meningitis while in hospital). The following factors are listed as the chief causes of difficulties in the diagnosis of miliary and meningeal tuberculosis: 1. The vagueness of the initial symptoms: the commonest were tiredness, irritability, and loss of appetite. Nutrition may be good, and the child may be neither feverish nor drowsy. Headache and vomiting were usually late symptoms. 2. In 18% of the children there was a history of an injury or infection immediately before the onset of symptoms. 3. In 25% meningism was absent. 4. In 42% a tuberculin-jelly test was negative. The Mantoux reaction was also frequently negative; in some it gave a confusing delayed reaction. 5. In 14% the initial level of sugar in the cerebrospinal fluid was 50 mg. per 100 ml. or more. 6. In eight children the meningitis was both purulent and tuberculous. 7. In some cases, proved at autopsy to be miliary tuberculosis, nothing abnormal had been seen on x-ray examination.

The author suggests that a Mantoux test (1 in 1000), and not a tuberculin-jelly test, be carried out when tuberculous meningitis is suspected. Particular importance is attached to a positive result in a child recently exposed to tuberculosis, for meningitis is more likely to develop in the six months after exposure than at any other time; and a positive result in a child under 2 years of age should always be taken as signifying active tuberculosis. At the same time a lumbar puncture is done, and, though usually the cerebrospinal fluid sugar level is 10 to 40 mg. per 100 ml., there are occasional variations. By a proper technique, acid-fast bacilli will be found in the smear in 90% of cases of tuberculous meningitis, and in the remaining 10% the organism will eventually be demonstrated by culture and guinea pig inoculation. The chest is examined with x-rays with the knowledge that a normal roentgenogram does not exclude tuberculosis. The diagnosis is then weighed in the light of the history, the physical examination, and the special investigations.

Clinical Features of Children Suffering from Neurological Sequelae of Rh Iso-Sensitization. C. Burton-Bradley. Australasian Ann. Med. 5:203-213 (Aug.) 1956 [Sydney, Australia].

While investigating the obstetric and developmental histories of children who were brought to the Spastic Center, New South Wales, three mothers stated that their affected child had suffered from jaundice at birth. Arrangements were made with the Red Cross Blood Transfusion Service for Rh investigations to be carried out in all cases of cerebral palsy as a routine etiological investigation. Eighteen children are here reviewed, who were brought along with many other cerebral palsied children to the Spastic Center outpatient department in search of help. All presented with varying degrees of slowness in the acquisition of sitting, standing, walking, and speech. The ages at which these 18 patients were presented ranged from 8 months to 8 years. Fourteen of the 18 children with icterus gravis neonatorum had been given blood transfusions, and 4 had not. The present age range of the patients is 5 to 14 years. Athetosis, high-frequency deafness, hypoplasia of the enamel of deciduous teeth, defective upward eye motion, specific peculiarities of gait, and discrepancy between estimable intelligence quotient and learning capacity are features. Seventeen patients are athetoids. In electroencephalographic investigations, 13 patients have normal records, 1 is borderline normal, and 4 have abnormal reccords.

Complications Following Intravenous BCG Vaccination of New-Born Infants: Re-Examination Three and One Half Years After Vaccination. M. R. H. Stoppelman and E. F. Drion. Nederl. tijdschr. geneesk. 100:2584-2591 (Sept. 8) 1956 (In Dutch) [Haarlem, Netherlands].

Of 1949 children who had been vaccinated during the neonatal period by intracutaneous administration of BCG, 1,608 could be reexamined 3½ years later. The Mantoux test in a dilution of 1:100 was positive in from 87.5 to 98% of all children. On the basis of the method of vaccination, the children fell into three different groups. Those of group 1 received two injections of 0.1 ml. of BCG vaccine; those of group 2 received two injections of 0.05 ml.; and those of group 3 received two injections of 0.03 ml. Suppuration of the regional lymph nodes occurred in 26.6% of the children of group 1; in 7.1% of those of group 2; and in 3.1% of those of group 3. In many children suppuration of one or more of the regional lymph nodes began 10 months or longer after BCG vaccination. Six children showed enlargement and seven showed suppuration of the regional lymph nodes 3½ years after BCG vaccination. In five children pus was aspirated and examined bacteriologically, but no acid-fast bacteria were isolated. Statistically significant differences were observed with regard to frequency of complications as well as with regard to negative tuberculin reactions in children grouped together according to the date of vaccination. The cause of these differences cannot be definitely established, but it is pointed out that studies in France revealed that vaccines prepared on different dates by the same laboratory were of varying potencies.

Early Puberty Due to Granulosa Cell Tumor of the Ovary. J. Picañol. Rev. españ. pediat. 12:309-318 (May-June) 1956 (In Spanish) [Zaragoza, Spain].

Granulosa cell tumors of the ovary are relatively frequent in women but very rare in girls of the prepuberal age. A girl began to menstruate at the age of 6 years. After the third menstruation there was scanty bleeding for 10 days. The child was undersized and underweight. Her mental and skeletal development were retarded. The abdomen was distended, the breasts were slightly enlarged and the areolas were pigmented. A free hard tumor was palpable at the hypogastrium. The uterus was enlarged, as felt by rectal palpation. Vaginal smears showed folliculin modified cells. There were no symptoms of virilism. A laparotomy revealed a large ovarian cyst. The removed cystic ovary measured 10 by 8 cm. The cystic fluid contained granulosa cells with marked lutein differentiation. Treatment against hypothyroidism was established two weeks after the operation. Menstruation did not occur any more. The breasts diminished in size and the areolas lost their deep pigmentation. A follow-up of 15 months revealed the child to be in good condition. Her weight, size, and skeletal development have greatly improved.

UROLOGY

Radium Therapy of Malignant Tumors of the Bladder: New Technic and Results. R. Darget. J. Internat. Coll. Surgeons 26:435-439 (Oct.) 1956 [Chicago].

One hundred one patients with malignant tumor of the bladder were given radium therapy in France between 1942 and 1954. Twenty of the 101 patients had a tumor that did not invade the submucosa (type 1), 50 had an extensive tumor situated near the ureteral orifices (type 2), and 31 had very serious malignant lesions that had invaded one-third to one-half of the bladder, with involvement of the ureters and the renal pelves (type 3). A five-year cure was obtained in 16 and a three-year cure in 17 of the 20 patients with type 1 tumor. A five-year cure was obtained in 32 and a three-year cure in 34 of the 50 patients with type 2 tumor. Results were less satisfactory in the patients with type 3 tumor, but their prognosis was the least favorable one. A five-year cure was obtained in a total of 49 of the 101 patients and a three-year cure in 53. When a patient had survived three years he had the best chance of a permanent cure.

The results obtained do not conform to the concept of other workers that the efficacy of radium therapy is necessarily limited to "favorable cases," i. e., in patients in whom the tumor has not invaded the bladder wall. The procedure used by the author for the treatment of all three types of malignant tumor of the bladder is as follows: 1. The radium needles must be accurately placed; a wide cystostomy, therefore, is required. Before the needles are inserted, the tumor is leveled as deeply as possible with the aid of surgical diathermy. 2. The radium needles must be kept in place during the entire period of radium therapy. This is best accomplished by reducing the automatic contractions of the bladder with procaine hydrochloride infiltration of the nervi erigentes and the pudendal nerves before the operation. 3. A special rubber balloon filled with a saturated solution of lead nitrate is placed close to the needles; this device prevents the needles from moving and acts as a screen against irradiation. 4. The radium needles are left in place for three or four days, and the cystostomy is maintained for about four weeks before the bladder is closed. 5. Extraperitonealization of the bladder makes operating much easier in cases in which the tumor is deeply situated and is difficult to expose. Extraperitonealization permits intravesical and extravesical implantation of radium to be done simultaneously. The ureters are exposed at the level of the superior strait. If the tracts appear greatly enlarged and unhealthy, a bilateral cutaneous ureterostomy is performed and the ureters fixed side by side at the median line, which permits convenient collection of the urine. When the condition of the kidneys and the ureter remains doubtful, a simple ureterostomy is performed on each ureter and a plastic ureteral sound of sufficient caliber is inserted and is pushed up to the renal pelvis. This drainage is maintained until the exact condition of the kidneys and whether they are capable of improvement becomes known. The simple ureterostomy will then be replaced by either a cutaneous ureterostomy or a ureterointestinal anastomosis.

The Present Position of Radical Cystectomy in the Surgical Management of Carcinoma of the Urinary Bladder. V. F. Marshall and W. F. Whitmore Jr. J. Urol. 76:387-391 (Oct) 1956 [Baltimore].

About 200 radical cystectomies for cancer of the urinary bladder have been performed in the departments with which the authors are connected. This report is concerned with the first 100 patients, who were operated on more than four years ago. The term radical cystectomy, as employed in this paper, includes even pelvic exenteration, 53% of the patients actually having undergone exenteration. Of the first 100 patients undergoing radical cystectomy, 41 lived four years after their first symptom of bladder tumor and 19 lived four years after the operation. The survival of these patients as a group was far less than their calculated average actuarial expectancy. Only about 4% of patients with untreated bladder cancer of high grade and stage survived four years from the first symptom. The authors gained the impression that the survival rates after radiation of carcinoma in stages C and D were quite low—much less than after surgical therapy. They are of the opinion that radical total cystectomy is advisable when the following combination of circumstances exists: (1) the cancer has extended through the muscle layer but cannot be demonstrated, even by laparotomy and nodal dissection, to have metastasized (i. e., cancers in stage C); (2) at least part of the neoplasm is located in the basal or rectal half of the bladder; (3) the patient would appear to have a life expectancy of four or more years if the cancer were not present; and (4) adequate facilities are available. Other circumstances may also warrant the use of this radical technique; but the above combination appears the most clearly defined, and it has not been a rare combination in the experience of these authors.

THERAPEUTICS

The Effect of Chlorpromazine on Hepatic Function and Morphology. J. K. DeVore, C. Daugherty and E. M. Schneider. Gastroenterology 31:391-398 (Oct.) 1956 [Baltimore].

Laboratory and liver biopsy studies were made on 12 patients who were being treated with chlorpromazine. Eight of the patients had received chlorpromazine in daily doses of from [illegible] to 3,500 mg. for 183 days without showing signs of jaundice. Hepatic function tests and liver biopsies failed to reveal [illegible] striking changes or consistent pattern that might suggest [illegible] induced abnormalities. The four patients in whom jaundice [illegible] develop had received considerably less chlorpromazine [illegible] much shorter periods of time than the nonicteric group. Liver biopsy performed on three of the four subjects with jaundice revealed plugging of the bile canaliculi. In two instances [illegible] portal infiltration occurred, and in the third instance irregular reduction of intracellular glycogen was noted. Laboratory studies in all four subjects reflected no hepatocellular dysfunction. The most notable abnormalities were increases in total serum bilirubin and in the serum alkaline phosphatase. However, more striking than these changes noted during the acute phase of jaundice was the fact that in every instance the cholesterol ester fraction increased as the patient's jaundice decreased. This occurred despite the fact that in two of the four subjects a "normal" cholesterol ester–total cholesterol ratio existed throughout the period of icterus. The alkaline phosphatase–total cholesterol ratio was abnormally high in three of the four subjects and may be of value as an index for the early diagnosis of intrahepatic obstructive jaundice. It is interesting to note that the jaundice cleared rapidly in all subjects despite the continued administration of chlorpromazine. A majority of the cases of chlorpromazine jaundice reported in the American and British literature similarly showed no evidence of hepatocellular d ease but did reflect a picture of "intrahepatic obstruction." It is concluded that chlorpromazine is not a specific hepatotoxin but is capable of eliciting unpredictable hepatic responses in susceptible patients.

Cortisone Therapy in Hepatic Cirrhosis. L. Bárbera. Riforma med. 70:1086-1090 (Sept. 22) 1956 (In Italian) [Naples, Italy].

Nineteen patients with hepatic cirrhosis were treated with cortisone or prednisone. Five patients received cortisone by mouth in doses of 100 mg. per day for the first 10 days and of 75 mg. per day for the following days. Nine patients received prednisone by mouth in doses of 20 mg. per day for at least 30 days. The doses were always equally divided throughout the 24 hours. Except for some cardiotonic drug, no other substance was added to the cortisone or to the prednisone. Bilirubinemia diminished and diuresis increased. Extreme oliguria (150 to 200 cc. of urine per day) was converted into polyuria of up to 3,000 cc. of urine per day. The following results were observed: the total protidemia varied moderately; there was a tendency toward the correction of disprotidemia even in patients who showed a decrease of total protidemia caused by hormonal treatment; and albumin and beta globulin tended to increase and gamma globulin to decrease. A transitory improvement marked by the return of consciousness was observed twice in two patients with hepatic coma.

Acute Glomerulonephritis Treated with Prednisone. L. Bertoni. Riforma med. 70:1091-1094 (Sept. 22) 1956 (In Italian) [Naples, Italy].

The author reports on seven patients with glomerulonephritis treated with prednisone. Good results followed in six patients. A marked effect was obtained in patients with the disease in acute or initial stages. Clinical symptoms tended to disappear and the urine became normal; the course of the disease was shortened considerably. The results were negative in a patient with a subchronic form of glomerulonephritis. The author believes that the effect of prednisone is more antireactive than antiphlogistic. The danger presented by old cortisone drugs of increasing the retention of water and salt in patients whose kidneys are diseased has been overcome by new cortisone derivatives.

Hypertension Treated with Rauwolfia Canescens: A Comparison with Rauwolfia Serpentina. R. W. P. Achor and N. O. Hanson. New England J. Med. 255:646-650 (Oct. 4) 1956 [Boston].

The authors investigated by clinical trial whether Rauwolfia canescens possesses any advantages over R. serpentina in the treatment of essential hypertension. Nineteen patients were selected from those who had participated in a previous study in which R. serpentina (whole root) was compared with reserpine in the treatment of hypertension. All were ambulatory patients whose average blood pressure exceeded 165 mm. Hg systolic, 90 mm. Hg diastolic, during an observation period of three or more months before the study. There did not appear to be any striking differences between the effects of the whole-root preparation of R. canescens and those of a similar preparation of R. serpentina. This similarity of results pertained not only to effects on blood pressure and pulse rate but also to side-effects. If any difference existed, it was that R. canescens tended to have fewer and less severe side-effects. In particular, it seemed to have less sedative effect than R. serpentina. Depressive reactions that have been observed among hypertensive persons treated with preparations of R. serpentina are also associated with the use of R. canescens. Continued use of R. canescens was well tolerated over a period of eight or nine months, and only when the dosage was increased did more troublesome side-effects develop. In patients who initially obtained a satisfactory reduction of blood pressure—about 40% of those treated—it was possible to maintain this improvement even though the dose was cut by half and given once daily instead of twice. There was no evidence in this group of the development of "resistance" to the drug. Patients whose blood pressure was not lowered appreciably by the use of R. canescens in moderate doses did not respond significantly when the doses were increased by 50%. This suggests that, if there has not been a satisfactory reduction in blood pressure after two months of treatment with moderate doses of R. canescens, it is unlikely that an increase in the dose will result in further benefit. If a good reduction of blood pressure has been obtained, it seems reasonable to expect that decreased dosage of the drug may continue to maintain the good response as well as to lessen the frequency and severity of side-effects. R. canescens is a potent pharmacological agent whose use should be carefully supervised.

PUBLIC HEALTH

Human Exposures in Populated Areas During Airplane Application of Malathion. P. E. Caplan, D. Culver and W. C. Thielen. A. M. A. Arch. Indust. Health 14:326-332 (Oct.) 1956 [Chicago].

A joint study was undertaken during the summer of 1955 by the California State Department of Public Health and the U. S. Department of Agriculture to determine the feasibility of using aerial applications of malathion on populated areas to control adult mosquitoes. Because such applications would mean communitywide exposures to an organic phosphate insecticide, the magnitude of the exposure involved in this type of operation was investigated. Malathion was applied over the small community of Planada (population 1,500) in the Central Valley of California. The spray material, containing 7.5% technical malathion, 4% no. 40 motor oil, 22% Shell solvent no. 2, and 66.5% medium grade diesel oil, was applied at the rate of 0.46 lb. of malathion per acre from an altitude of 70 ft. It was discharged through no. 4 spray nozzles from a boom under the wing of a light airplane. Human exposure was measured by air-sampling and surface-deposit measurement techniques. These measurements were made in the open and inside buildings. The spray had a mass-median diameter of 109^{μ}. Comparison of air-sample measurements with surface-deposit measurements indicates that air sampling measured only 12% of the insecticide present in the outdoor atmosphere. This 12% probably represents inspiratory exposure. A man working in the open received an inspiratory exposure about five times greater than that of a man working inside a building. The outdoor skin exposure was roughly four times the indoor exposure. During the complete operation of airplane spraying of a small town, the total exposure of a man working outdoors was such that, when calculated on a milligram per kilogram basis, his inspiratory and skin exposures would have had to be multiplied by factors of 500,000 and 120,000, respectively, to approach $L.D._{50}$'s of experimental animals. On the basis of these findings, the application of malathion in amounts used in this study constitutes no hazard to the normal human population.

Antigenic Potency of Poliovirus Vaccines. S. Kelly and G. Dalldorf. Am. J. Hyg. 64:243-258 (Sept.) 1956 [Baltimore].

The commercial vaccines used in the state of New York during the summer and fall of 1955 were evaluated by Gard's method and the results related to other potency values, e. g., ratio value in the monkey potency test, and antigenic response in man. Some of the factors influencing estimates obtained by the test were also studied. Potency differences were detected varying from a few vaccines with no detectable potency to a few with high potency, with up to six-hundred-fold differences between these extremes. Many vaccines appeared to have greater type 3 than type 1 antigenicity. Vaccines potent by the guinea-pig test were also potent by the monkey test. The differences in potency apparent in the animal tests were not detected in a small-scale study of the serologic response of human beings to the vaccines. Factors found to influence potency values occurred chiefly in the neutralization test and included size of virus dose, choice of tissue-culture indicator, and length of observation period. Factors found to exert little or no effect on antibody production were animal weight and sex. Storage of serum at refrigerator temperature and in a frozen state before testing did not affect potency values. Vaccines stored for several months had potency values that were lower than previously estimated values. The authors also describe a simplified modification of Gard's test.

BOOK REVIEWS

Athletic Injuries: Prevention, Diagnosis and Treatment. By Augustus Thorndike, M.D., Chief Surgeon to Department of Hygiene and Department of Athletics, Harvard University, Boston. Fourth edition. Cloth. $4.50. Pp. 252, with 113 illustrations. Lea & Febiger, 600 S. Washington Sq., Philadelphia 6, 1956.

The appearance of a new edition, the first in eight years, of this valuable work, originally published in 1936, coincides with greatly increased interest in the various medical aspects of athletics by physicians in the United States. The book has been so thoroughly revised that it is virtually new. Many of the excellent line drawings are new, and all of the illustrations are well done. The chapter on physical therapy has been entirely rewritten, and the one on physical fitness has been brought up to date. There is an ample bibliography drawn principally from American and English literature.

The first part is devoted to a discussion of the prevention of athletic injuries. It contains sections on the nature of and determination of physical fitness, including a discussion of the physiochemical changes and one on physical training. In discussing physical fatigue and aids in the prevention of injury, the author points out that the use of oxygen and various stimulants or "pep pills" has never been shown to improve athletic performance, whereas the abuse of these drugs may cause both physical and psychological harm. Part 2 discusses the common types of athletic injuries, and separate chapters are devoted to sprains, strains, contusions, fractures, dislocations, internal injuries, infections, inflammations, lacerations, and abrasions. The author points out that the description of a sprain should include accurate localization of the ligament involved, even though it may be necessary to revise this observation from day to day as treatment progresses. His finding that a sprain of the anterior tibiofibular ligament is the most common ankle sprain is at variance with other reports, but it appears to be based on careful, accurate observation. It is interesting to note that sprain of the tibial collateral ligament of the knee occurs four times as often as the next most common sprain. The discussion of muscle strains is excellent. Part 3 is devoted to the diagnosis and treatment of the more common regional injuries. It concludes with a chapter on physical therapy and reconditioning. The author finds that the bones most commonly broken are those of the fingers and hands, with those of the face a surprising second in incidence, preceding leg, wrist, and foot fractures. The facilities at the Harvard field house, which provide the opportunity to make roentgenograms and set simple fractures under anesthesia, make possible ideal early treatment for these serious athletic injuries.

There is room for some difference of opinion with regard to the value of the hypochlorite foot bath recommended for the prevention of epidermophytosis. The drop in incidence of this infection during the football season, cited by the author, could be due to the effect of physical training and improvement in general hygiene during this period. The use of 10% ammoniated mercury ointment and boric acid salve for the treatment of impetigo is probably outdated. Bursitis is discussed briefly, and no mention is made of x-ray therapy for this condition. Sprain of the sacroiliac joint is a questionable diagnosis when there are so many other possible causes of low back strain. The view that shin splints represent a muscle tear and that they must be treated by rest is at variance with the experience and practice of most runners and track coaches. The conclusions of the Kaplan-Browder study of prize fighters are not quoted fairly. These are only minor faults in an excellent and valuable reference book for any physician treating school, college, or professional athletes.

Speech Handicapped School Children. By Wendell Johnson, *Ph.D., Professor of Speech Pathology and Psychology,* University of Iowa, Iowa City, et al. Second edition. Cloth. $4.50. Pp. 575, with 8 illustrations. Harper & *Brothers,* 49 E. 33rd St., New York 16, 1956.

The book is a comprehensive survey of the speech disorders of children as seen from the standpoint of the educator. It is essentially a textbook for training teachers and speech therapists. The first two chapters present a general orientation and Johnson's point of view. The clinical point of view in education is stressed. The plea here is for increasing recognition in the school of all aspects of the child's development—physical, emotional, and educational—with particular attention to individual differences. Abundant statistical information is given to support the thesis that speech-handicapped children are an important part of the community. Therefore, they are worthy of a concerted effort on the part of the school personnel to correct the deficiency that so seriously interferes with communicative needs of such children. Each of the various types of speech disorders is dealt with in a separate chapter. A chapter contributed by S. F. Brown is devoted to the speech problems encountered in children with cleft palates and cerebral palsy. The aphasias are not considered. The longest chapter, reflecting Johnson's special interest, is devoted to stuttering. A chapter on the speech handicap of children with impaired hearing was contributed by Jacqueline Keaster, an audiologist.

Johnson's point of view toward children with speech disorders seems to be a useful one for teachers, and, as might be expected, the other contributors generally reflect the same point of view. Johnson is devoted to his subject and succeeds rather well in communicating his enthusiasm. In the chapter on stuttering, he dwells at length on the emotional aspects of stuttering, defines the disorder as a "type of anxiety-tension," and states that stuttering is an anticipatory apprehensive, hypertonic avoidance reaction. This point of view is probably useful for the educator, but, since the book does not include any analysis of therapeutic results, the reader is left with many unanswered questions. Johnson protests too much against the inclusion of stuttering in the category of neurotic symptoms. He devotes many pages to trying to protect his stutterers from the neurotic label. In this discussion he is not too successful and only manages to get involved in semantic arguments. This need not detract from the value of his contribution to education. Certainly it would be unfair to evaluate the book as a medical or psychiatric textbook, since this it is not and makes no claim to be.

The Labyrinth: Physiology and Functional Tests. By Joseph J. Fischer, M.D., Clinical Professor in Otolaryngology, School of Medicine, Tufts University, *Boston.* Cloth. $6. Pp. 206, with 30 illustrations. *Grune & Strat* Inc., 381 Fourth Ave., *New York* 16; 99 Great Russell St., London, W.C.1, England, 1956.

Knowledge about the labyrinth has increased in the last few decades to a scale unthinkable even a short time ago. From a viewpoint of function, the labyrinth is divided into cochlear and vestibulosemicircular parts and the study of each of these divisions has been developed into an advanced discipline. Although this book is entitled "The Labyrinth," it deals with facts and problems of only a small, nonacoustic part of this organ. Its real objective is to summarize the methods presently available for testing the vestibular apparatus. To help the reader understand the subject, the first chapter is devoted to a brief survey of vestibular physiology. The second chapter is concerned with the common vestibular symptoms and phenomena that are elucidated by the laws and theories of vestibular function. All vestibular reflexes and clinical signs, such as vertigo, nystagmus, and other spontaneous signs, and the induced reactions, such as past pointing, optokinetic reaction, calorization, rotation, and mechanical and galvanic reactions, are discussed and their origin explained. Chapter 3 is devoted to a presentation of the *functional* tests. The points, discussed from a physiological viewpoint in the previous chapter, are presented entirely from the

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

viewpoint of their clinical applications. The various methods of testing the vestibular apparatus are considered under the heading of Induced Reactions. This part of the book is comprehensive and modern in its concepts. The newer developments and modifications in the caloric and rotatory stimulation are presented and briefly explained. The techniques of performing these tests are given, and the evaluation of the findings is discussed. The reader can readily familiarize himself with the newest testing methods, for example, directional preponderance, culmination test, and cupulometry. Each section contains adequate references. At the end of the book is a survey evaluating the abnormal results of various test performances, and a differentiation is made between peripheral and central vestibular lesions. Vestibular testing and labyrinthine evaluation have never enjoyed their deserved popularity within the field of otolaryngology. This volume can be heartily recommended to physicians, from the first year otolaryngological resident, who should profit greatly from it, to the experienced practitioner.

Essential Urology. By Fletcher H. Colby, M.D., Consultant, Massachusetts General Hospital, Boston. Third edition. Cloth. $8. Pp. 656, with 358 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1956.

The fact that this third edition has been published within six years of the first attests to the author's ability to provide a text that keeps abreast of current diagnostic and therapeutic methods in urology. The book is divided into three parts. Part 1 deals with the embryology, anatomy, and physiology of the genitourinary organs; part 2 with examination of the urologic patient; and part 3 with diseases of the genitourinary organs. The first part is concise and factual. The development, adult relationships, and functions of the various organs are correlated so as to give a clear and accurate picture of the genitourinary system in health and disease. Drawings and photographs help to illustrate the subject matter. Where applicable, paragraphs called "practical considerations" point out salient facts that are clinically important. Part 2 is brief and touches on significant points in a patient's history and physical examination. Reference is made to a few laboratory tests as well as to cystoscopic and urographic studies. Part 3 constitutes about four-fifths of the volume. Beginning with the kidneys, each organ of the urinary tract is treated individually and consecutively. Each disease is introduced in broad general statements concerning the process. The lesions encountered are then reviewed, including both gross and microscopic features. Characteristic symptoms are considered and followed by the diagnostic methods that apply. Finally, treatment is reviewed and the prognosis outlined. In general, the subject matter is clearly and concisely presented in a readable fashion. Illustrative urograms and photographs demonstrating gross and microscopic pathology are used generously. In discussing topics on which multiple opinions or methods of management prevail, the author recognizes these differences and gives his own preferences. This edition should be of value, particularly to the medical student, the graduate student in urology, and the general practitioner. An extensive bibliography of current literature is provided.

New Bases of Electrocardiography. By Demetrio Sodi-Pallares, M.D., Chief of Department of Electrocardiography at National Institute of Cardiology of Mexico, Mexico City, with collaboration of Royall M. Calder, M.D., editor, English translation, Clinical Professor of Medicine, Graduate School, Baylor University, Houston, Texas. Translated from recent revision of third Spanish language edition, copyright by La Prensa médica mexicana, México 7, D.F. Cloth. $18.50. Pp. 727, with 523 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3, 1956.

This English edition of a textbook on electrocardiography that has already had three Spanish editions is most welcome. The book is written primarily for students and incorporates within it the many years of teaching experience that the author has had at the National Institute of Cardiology of Mexico. For instance, one will find in this book the clearest explanation of the electrical position of the heart given anywhere. Although the author follows the lead of his teacher, the late Dr. Frank Wilson, he has also included results of his own research, particularly in reference to the correlation of electrocardiographic, clinical, and pathological data. The first chapters follow the conventional pattern of describing the electrophysiological basis for electrocardiography. Subsequent chapters are more concerned with the direct application of these principles than with the long detailed descriptions of clinical electrocardiography commonly found in most textbooks. Vectorcardiography, the ventricular gradient, and intracavitary potential are discussed thoroughly, each in separate chapters. The mathematics of electrocardiography is elaborated in an appendix. The text is well illustrated with diagrams and electrocardiograms. Although there is an excellent bibliography, a great deal of its effectiveness is lost because there is no correlation with the text. This book is recommended to the students and physicians who wish to learn the basic concepts of electrocardiography. No clearer presentation of these is available. It is also an excellent reference book for the cardiologist who from time to time needs a little refreshing in his field.

The Initial Management of Thoracic and Thoraco-Abdominal Trauma. By Lawrence M. Shefts, M.D., Thoracic Surgery Consultant to Brooke Army Hospital, Fort Sam Houston, Texas. Publication number 265, American Lecture Series, monograph in Bannerstone Division of American Lectures in Surgery. Edited by Michael E. DeBakey, M.D., Professor of Surgery and Chairman of Department of Surgery, Baylor University College of Medicine, Houston, Texas, and R. Glen Spurling, M.D., Clinical Professor of Surgery, University of Louisville, Louisville, Ky. Thoracic Surgery Division, editor: Brian B. Blades, M.D., Professor of Surgery, George Washington University, Washington, D. C. Cloth. $6.50. Pp. 121, with 18 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1956.

The background of this monograph is the experiences of the author during World War II. The author discusses resuscitation, thoracic wounds, thoracoabdominal wounds, wounds of the thoracic wall, and closed thoracic and thoracoabdominal trauma and includes illustrative cases. Resuscitation of the patient is foremost in the author's planned program of treatment. The pathogenesis, physiology, and pathological findings are emphasized. The author warns against panicky decisions and against stampedes to the operating room. As surgeons gained experience in the battle zone, fewer thoracotomies were performed. Technical considerations were intentionally omitted from the book. Preference was given to discussing the indications for, and the timing of, surgical operations. The illustrations and line drawings are well placed, graphic and clear and carry easily understood legends. The bibliography is up-to-date and authoritative. The illustrative cases are unusually illuminating; they represent each type of injury discussed in the monograph. With the increases in automotive travel and in the power and speed of vehicles, the number of severe injuries is increasing. This timely monograph is recommended for all physicians, particularly those who serve in the emergency rooms of hospitals.

Principles and Methods of Sterilization. By John J. Perkins, M.S., Director of Research, American Sterilizer Company, Erie, Pa. Cloth. $8. Pp. 340, with 174 illustrations. Charles C Thomas, Publisher, 301-327 East Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1956.

This volume was written to help persons who are responsible for sterilization in hospitals, but it could serve as a general guide for sterilization techniques. It integrates basic principles with practical methods for sterilization of materials. The principles and methods discussed, however, will also be of interest to physicians and surgeons, clinical instructors, pathologists, bacteriologists, and laboratory technicians. The first chapters contain a brief historical introduction and much of the basic material on sterilization and on the equipment used. Subsequent chapters deal with the practical aspects of sterilizing dressings, dry goods, rubber goods, surgical instruments, syringes, and needles. Various methods of disinfection and sterilization and their limitations are discussed, including the use of steam, dry heat, boiling water, chemicals, and gases. In other chapters are discussions on control techniques, central supply departments for hospitals, and preparation of parenteral solutions and infant formulas. References are included at the end of each chapter, and the book also contains a general subject index. The volume should be a valuable addition to the library of any person responsible for sterilization.

QUERIES AND MINOR NOTES

ATHEROSCLEROSIS

To the Editor:—*Please discuss the relative values of products containing choline, methionine, inositol, and Cytellin in the treatment of atherosclerosis and arteriosclerosis. What clinical proof is there showing the value of treating hypercholesteremia for preventing atherosclerosis and arteriosclerosis?*

Harry G. Kurz, M.D., La Habra, Calif.

Answer.—Choline, methionine, and inositol added to a normal, adequate diet are without effect on hypercholesteremia both experimentally in animals and clinically. They are equally ineffective in preventing cholesterol-induced atherosclerosis in animals. The sitosterols, like Cytellin, if given in large doses are capable of reducing cholesterol-induced hypercholesteremia and atherogenesis. Clinically they are useful in decreasing hypercholesteremia and in slightly depressing normal cholesterol levels. The effect, however, is not uniform in all patients so treated, some reacting more favorably than others. Generally, the higher the cholesterol level, the more pronounced the effect. At the present time there is no direct clinical proof that depressing hypercholesteremia helps to prevent the development of atherosclerosis. The justification for the use of these agents lies in the well-documented fact that diseases accompanied by hypercholesteremic states have a significantly higher incidence of atherosclerosis, particularly of the coronary vessels, than diseases accompanied by normocholesteremic states. Also, patients with coronary artery diseases, as a group, have elevated serum lipid levels. It is theoretically sound (and experimentally proved) to implicate the serum lipids in atherogenesis and therefore to try to reduce abnormally high serum lipid levels by dietary or pharmacological means in the hope of retarding the vascular process.

ULCER PILLS

To the Editor:—*Please give information on Exul, which is used to heal ulcers.*

M.D., Illinois.

Answer.—Exul is labeled to be a mixture of nupra (nonhormonic, nonsteriadic extract of cattle organs—liver, brains, adrenals, etc.), 2 gm.; dehydrated milk and cream, 15 gm.; choline hydrochloride, 30 mg.; ascorbic acid, 5 mg.; niacinamide, 1.2 mg.; thiamine hydrochloride, 0.6 mg.; vitamin B_{12}, 0.0009 mg.; and ferrous gluconate, 0.009 gm., with flavor of cocoa, milk solids, and sucrose added.

RICKETS WITH SO-CALLED ADEQUATE DIET

To the Editor:—*Is it possible to develop rickets despite prenatal calcium supplements, large amounts of milk throughout the first two years, and adequate doses of vitamin supplements in infancy? Is there any way, at this time, of definitely proving by x-ray or other means the presence or absence of rickets now or then?*

M.D., New York.

Answer.—It should be emphasized that rickets has now become a rare disease in the United States. During the early part of the century, most cases of marked knock knees were thought to be due to rickets. Now the burden of proof would be on anyone ascribing knock knees and other bone deformities to rickets. In any case the diagnosis of rickets should never be made on the basis of bone deformities alone. Genu valgum may be the result of numerous causative agents, and in most instances hereditary factors are responsible. Mild knock knee is commonly seen in young children and is considered physiological. Marked genu valgum may occur in patients with eccentro-osteochondrodysplasia (Morquio's disease), lipochondrodystrophy (Hurler's syndrome), or various forms of rickets; after poliomyelitis; or as a result of trauma to the lateral femoral epiphysis or the proximal tibial epiphysis. Thus accurate differential diagnostic studies must be carried out. To answer the first question specifically: a normal infant would never develop rickets on adequate prenatal and postnatal diets. There are, however, some forms of rickets that develop in spite of so-called adequate diets. These are vitamin D-resistant rickets (Albright), osteodystrophy (renal rickets), the Fanconi syndrome, celiac rickets, and cystinosis. All these conditions are usually associated with dwarfism and present other signs and blood disturbances that make their diagnosis possible.

In answer to the second question, the presence of rickets if still active could be definitely proved by the laboratory findings of low serum phosphorus level, normal or low serum calcium levels, and increased alkaline phosphatase. The x-ray manifestations at the wrist and knee would be very typical, with cupping, fraying, and flaring seen at the ends of the bone. Recently healed rickets would show the new deposits of calcium at the end of the bones, but the blood findings would be normal.

DIABETIC RETINOPATHY

To the Editor:—*Please discuss the relation of high-animal-protein diet, Propadrine, and vitamin B_{12} in diabetic retinopathy.*

Frederick E. Mott, M.D., New Haven, Conn.

Answer.—It is well known that the serum albumin level tends to be low and the beta globulin fraction frequently high in diabetes, particularly in patients whose glycosuria is poorly controlled and in those suffering from retinopathy and nephritis. It has been reported that, among a group of adequately treated diabetic patients with abnormally low levels of serum albumin, several exhibited an increase in these levels some weeks or months after the ingestion of a diet containing 120 to 140 gm. of protein daily. All of these are said to have experienced remission of retinopathy as judged by improvement in visual fields and visual acuity and cessation of hemorrhages. The implication that the return of serum albumin toward normal levels, occasioned by the high-protein diet, was responsible for the retinal improvement may be justified, and certainly the administration of such a diet, in the absence of renal failure, would be harmless. On the other hand, it must be recognized that the etiology of diabetic retinopathy is still unknown, and it has not been proved to be caused by low concentrations of serum proteins. Furthermore, because of the frequency of spontaneous remissions in the retinal lesions, it is very difficult to be certain whether improved visual acuity and cessation of hemorrhages are in fact attributable to the treatment employed. Perhaps the high-protein diet should be regarded as a means of attempting to correct low levels of serum albumin rather than as a treatment for retinopathy itself. Propadrine is a vasoconstrictor and bronchial dilator and would not be expected to be beneficial in diabetic retinopathy. Becker and co-workers have found that, after receiving a test dose of vitamin B_{12}, diabetics with retinopathy excrete nearly five times as much of the vitamin as do diabetics without retinopathy and approximately twice as much as nondiabetics. These observations should be regarded for the present as uncovering an interesting and possibly significant anomaly of vitamin B_{12} metabolism in such patients, but they do not demonstrate that treatment with vitamin B_{12} is beneficial. This has not been convincingly shown by any investigations to date. The medical management of this condition continues to be most unsatisfactory, except for measures aimed at the strict control of hyperglycemia and glycosuria, and even these are frequently unsuccessful.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

SEDATIVE ACTION OF ALCOHOLIC BEVERAGES

To the Editor:—*Could you give information on the sedative action of liquors (i. e., whisky, rum, vodka)? For example, would it be correct to say that a jigger of whisky might have the same effect as ½ grain (30 mg.) of any of the barbiturates?*

Royal A. Meyers, M.D., Watertown, Conn.

Answer.—The sedative action of an alcoholic beverage does not depend on the flavor of the drink but on the amount of alcohol consumed. Although the sedative effect of alcohol somewhat resembles the action of barbiturates and when both are consumed a definite synergistic effect occurs, it would be a mistake to consider their effects to be identical. Measurable effects of alcohol occur when the alcohol in two ordinary drinks (about 30 gm. of absolute alcohol) has accumulated in the body of an average-sized (150 lb. [68 kg.]) individual. The chief objective symptoms would then be measurable loss of judgment and deterioration of vision. Barbiturates produce their threshold effects of moderate narcosis with about 30 mg. (½ grain). The ratio of the weight of alcohol to the weight of barbiturates for threshold effects would then be about 1,000 to 1. When fatal dosages of alcohol and barbiturates are compared, this ratio is about 100 to 1. This approximation is arrived at by comparing a fatal dose of accumulated alcohol of about 320 gm. (400 cc., or the alcohol in 26 ordinary drinks) to the fatal dose of barbiturates—about 3.3 gm., or 50 grains.

OSTEOMYELITIS

To the Editor:—*A patient has had osteomyelitis of the right femur since he was 7 years old and he is now 46 years old. He has been operated on seven or eight times, the last operation having been performed on May 9, 1956. The infection extends into the distal end of the femur, and there is always a small amount of foul-smelling drainage from the wound. Since it is necessary to take medicine for relief of pain in the leg at intervals every day, he is considering amputation. Is there any possibility of bone grafting where approximately three-fourths of the femur would have to be removed? The upper one-fourth of the femur is not involved in the process.*

Howard V. Weems, M.D., Sebring, Fla.

Answer.—In osteomyelitis, resection of the femur and replacement by bone graft is not very satisfactory. Such grafts can be resorted to for filling old osteomyelitis cavities, if the infection can be brought under control. They will prove successful very often, but the success depends on whether there is enough soft tissue to cover the cavity adequately. The difficulties encountered in a case of this sort might be so great that amputation would be indicated, but such decision would depend on many factors, such as the type of organism causing the trouble, whether the organism is responsive to any of the antibiotics, and the amount of soft-tissue scar.

HISTOPLASMIN SKIN TESTS

To the Editor:—*In case of a positive histoplasmin skin test, what is the chance of false-positive reaction (1) in persons with negative skin tests for other fungi (coccioidin or blastomycin) or (2) in persons with positive tests for other fungi? Does the negative serology for histoplasmosis in the presence of a positive histoplasmin skin test and clinical evidence of obscure pulmonary disease of unexplained lymphadenopathy exclude (1) histoplasmin infection or (2) active stage of histoplasmosis? Please discuss the comparative value of the following serologic reactions in the diagnosis of active histoplasmosis: (1) complement fixation, (2) precipitin test, (3) agglutination, and (4) collodion agglutination.*

M.D., Ohio.

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—Histoplasma infections may result in skin-test sensitivity to other fungus antigens. Occasionally an individual may react strongly to histoplasmin but to a much lesser degree to blastomycin, usually less than 50% of the histoplasmin reaction, and coccidioidin rarely. A false-positive reaction to histoplasmin does not occur in persons with negative skin tests for other antigens. In persons with positive tests to other fungi as well, sensitivity to the homologous antigen, histoplasmin, is much greater than to the other antigens; therefore, the positive test becomes significant and is not to be considered a false-positive reaction. Thus it is wise to test for comparative purposes all three antigens: histoplasmin, coccidioidin, blastomycin (and also tuberculin, which does not produce cross reactions) at the same time. Negative serology, particularly the complement-fixation test, in the presence of a positive skin test for histoplasmin and clinical evidence of obscure pulmonary disease and unexplained lymphadenopathy could mean (1) that it might have been too early for antibodies to have formed, (2) that dissemination was occurring and antibodies had disappeared, or (3) that the positive skin test and the clinical condition were unrelated, that is, the positive skin test represented a mild or healed primary infection in the presence of some other disease. In the latter case, in all probability active histoplasmosis was not present. It must be remembered that the complement-fixation test is negative in about 10% of patients with active histoplasmosis and that about 8% of normal individuals have antibodies in low dilution. Serial complement-fixation tests should be done, as a change from a negative to a positive would be significant.

The complement-fixation test is the most valuable and practical serologic test for the diagnosis of active histoplasmosis. Serial tests should be made. In active infection, a rise in antibodies occurs with a peak during the second and third week of the disease and a gradual falling off at four to eight months. A low antibody titer early in the course of the disease may signify a poor prognosis (dissemination) and a high titer a self-limited disease with a good prognosis. In mild cases, the rise in titer is transitory, and, in more severe cases, antibodies may persist for a long time. Antibodies are absent or negligible in serums of patients with apparently only cutaneous or mucocutaneous lesions. Cross reactions rarely occur with an antigen of Coccidioides immitis in the complement-fixation test but not uncommonly occur with Blastomyces dermatitidis. However, in the latter, the complement-fixation titer rises with progression and remains elevated throughout the terminal stages; on the other hand, in focal lesions and cutaneous infections, the complement-fixation titers are low or absent. Precipitin and collodion agglutination tests are sometimes positive in milder cases in which complement-fixation antibodies have not developed. Because these tests may become negative in cases of long duration and because they are sometimes positive in early ones, regardless of whether coccidioidin, histoplasmin, or blastomycin is employed, some workers use all three tests in their laboratory in order to get the most information.

Answer.—The skin-test antigens (histoplasmin, blastomycin, coccidioidin, and haplosporangin) manifest varying degrees of cross reaction. Furthermore, the antigens currently in use have not been truly standardized, either against a homologous standard or against comparative standards. Therefore, comparison of test findings from other sources and their interpretation in relation to a given clinical case is not permissible on the basis of present-day information. The answer is "no" to both parts of the second question. Various types of serologic findings have been observed in known cases of histoplasmosis: (1) no detectable antibodies and (2) antibody dynamics with a rise and fall in titer during acute illness and the convalescent period. In some instances, the titer may wane but persist at low levels for years, while in the majority it tends to fall and disappear in about six months or so after the onset of infection. Patients with chronic pulmonary cavitary histoplasmosis are more likely to have prolonged persistence of detectable complement-fixing antibodies. On the other hand, tests on serums from some 50% of patients with disseminated histoplasmosis have been consistently negative. It should be apparent, then, that negative results with presently available serologic tests cannot be used to exclude prior or active infection with Histoplasma capsulatum.

There is much disagreement as to the value and accuracy of the serologic reactions in the diagnosis of active histoplasmosis. At present, complement-fixation tests with *yeast-phase antigens* appear to offer the most consistent results in tests on serums from experimentally infected animals. However, there have been no large-scale comparative studies involving all four types of tests listed. There are serious discrepancies in findings with different forms of antigen, for example, between yeast-phase and mycelial filtrate (histoplasmin) antigens in complement-fixation tests on the same serums. The picture is further confused by the cross reactions of serums positive for H. capsulatum with other fungus antigens and vice versa. In addition, the lack of standardization and uniformity of techniques among the various workers makes comparison of results relatively meaningless at present. It appears reasonable to conclude, however, that the detection of an antibody response with a "standardized" Histoplasma complement-fixation technique may, at least, permit the clinician to draw the diagnostic inference that the patient has been infected with one of a group of fungi that elaborate a common antigen. It should be emphasized, as indicated above, that failure to detect such an antibody response does not exclude fungal infection. Thus, demonstration of characteristic yeast forms in sections of biopsy material and/or isolation and identification of the organism remain the only certain means of establishing the specific diagnosis of histoplasmosis.

LOSS OF WEIGHT

To the Editor:—*Is there any drug or compound that will cause a loss of excess weight without the need of a strict diet? I am aware of the amphetamine compounds to lessen the appetite, but I would like to know of something else to use for this problem.* *T. J. Bluechel, M.D., Surfside, Calif.*

Answer:—No known drug or compound may safely be taken to cause loss of weight. The word safely deserves emphasis, since some drugs such as alphadinitrophenol, which have succeeded in taking off pounds, have had the disadvantage of making some people blind and killing others. Various diets have been suggested for obesity, including one comprised largely of protein, another comprised largely of fat, and one comprised largely of carbohydrate. There is no evidence that any one of these diets, or any other treatment of any kind, avoids the basic laws of energy exchange. In other words, all fat comes from food, and the only way an obese individual can lose weight is by eating less and exercising more. In this answer the more important question is not mentioned: What is it in an individual's life and make-up that gives him the appetite to cause obesity?

ALLERGY ASSOCIATED WITH MENSTRUATION

To the Editor:—*Please give information on the occurrence of allergic phenomena associated with menstruation. A patient aged 33 has urticaria (hives) with menses.*

Robert Z. Collings Jr., M.D., Casa Grande, Ariz.

Answer.—Allergic reactions such as skin diseases, asthma, and hay fever frequently occur in the premenstrual period and are usually associated with symptoms of premenstrual tension. Several theories concern the etiology of this condition. One of them postulates that the symptoms of premenstrual tension are the result of changes in the electrolyte and water balance of various tissues of the body, which are probably the result of cyclic ovarian activity. According to Zondek and Bromberg (*J. Obst. & Gynaec. Brit. Emp.* 54:1, 1947), allergic hypersensitivity to the steroid hormones or to the products of their metabolism excreted in the urine can be shown in certain pathological conditions generally related to menstruation or to the menopause by means of active cutaneous tests. Steroid hormones (estrogen, estradiol, progesterone, pregnandiol, testosterone, androsterone, and corticosterone), as well as prolan (chorionic gonadotropin) and insulin, were found capable of allergenic activity. The clinical manifestations of endocrine allergy can be the same, although the hormonal allergen may vary in different cases.

The following varied range of clinical manifestations may be due to endocrine allergy, though they need not necessarily be of this origin: (1) in the respiratory tract—asthma and vasomotor rhinitis; (2) in the cutaneous system—angioneurotic edema, chronic urticaria, and acne; (3) in the nervous system—migraine; (4) in the genital system—premenstrual tension and pruritus vulvae; (5) in the digestive system—nausea, vomiting, diarrhea, and epigastric pain during the premenstrual phase; and (6) in the ocular system—chronic recurrent conjunctivitis and certain forms of keratitis. Heckel (*Am. J. Obst. & Gynec.* 66:1297, 1953) states that the results of pregnanediol therapy tend to support the hypothesis that many disorders related to ovarian function—premenstrual distress, menopausal symptoms, ovarian pain syndrome (congestion-fibrosis syndrome, pelvic hyperemic syndrome), painful breasts and chronic cystic mastitis, some endometriosis and hypogonadism, and headache and dermatoses associated with the menstrual cycle—are caused by endogenous allergy to steroid hormones. Patients with these disorders were found to be sensitive to pregnanediol, a metabolic product of progesterone with no known biological activity. Pregnanediol produced systemic reactions resembling those already experienced, as well as local reactions to large doses.

LENSES FOR PATIENT WITH DEGENERATION OF MACULA LUTEA

To the Editor:—*A 29-year-old white man has complete degeneration of the macula lutea. The peripheral vision in both eyes is normal. Placental implants have been surgically placed in both retinas, with the hope of staying the progression of the degeneration in the macula area to the periphery of the retina. Is there some place in the United States that is able to make glasses for reading for such a patient? Clinical vision is 20/300 bilateral.*

Paul W. Hughes, M.D., Fort Lauderdale, Fla.

Answer.—It is not necessary for your patient to be sent to a special place in the United States for testing to see whether he can be helped. Magnifying lenses and devices offer the only means of making your patient able to read. Such devices and lenses are available to everybody through the American Foundation for the Blind, Inc., 15 W. 16th St., New York 11. They will send you on request their booklet of devices for helping such patients, and you can make the test yourself in your office. However, it is not at all predictable whether a person with 20/300 vision can be helped. These cases are individual, and one must make the tests rather than predict an outcome.

INGROWN TOENAIL

To the Editor:—*A woman is troubled with ingrown toenails on both great toes. Two years ago a surgeon removed the medial half of each nail, but the nails grew back and turned in as much as before, or more. Today she has much tenderness, pain, and discomfort, so that she is unable to walk any distance, nor can she wear heels that throw her weight on the great toe. Kindly advise if any operation has been devised that will give permanent relief for ingrown toenails.*

M. D., New Jersey.

Answer.—To prevent the recurrence of an ingrowing toenail, it is necessary not only to remove a section of the nail but to completely eradicate the nail bed of that section. The technique for this procedure has been described by several authors: "Diseases of the Foot," by Emil D. W. Hauser (Philadelphia, W. B. Saunders Company, 1950); "The Foot and Ankle: Their Injuries, Diseases, Deformities and Disabilities," by Philip Lewin (Philadelphia, Lea & Febiger, 1947); and "Functional Disorders of the Foot: Their Diagnosis and Treatment," by Frank D. Dickson and Rex L. Dively (Philadelphia, J. B. Lippincott Company, 1939).

CESAREAN SECTION IN PATIENT GIVEN PENTOTHAL

To the Editor:—*I would like to add to the answer given to the Query and Minor Note entitled "Cesarean Section in Patient Given Pentothal" in* The Journal, *Oct. 13, 1956, page 698, a reference to the report by Martland and Martland* (Am. J. Surg. *80:270, 1950). These authors showed that instead of a placental barrier there is a pooling tendency in the fetus for most of the sedatives given the mother by the oral, rectal, parenteral, or inhalation route. By actual analysis the barbiturates, for example, were found to accumulate in the fetus to a level almost twice that present in the mother, because of the slower and less efficient detoxification and excretory mechanisms of the fetus.*

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« Washington News »

Salk Vaccinations Urged for Holidays • •
Congressional Interest in Jenkins-Keogh Bills • •
Army, Air Force Report on Residencies • •
First Small Business Loans to Hospitals • •
VA Studying Tuberculosis Infection • •
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POLIOMYELITIS VACCINE

Two more developments at the federal level have stressed anew the problems in the Salk poliomyelitis vaccine situation. The Public Health Service now estimates a manufacturers' backlog of close to 23,000,000 cc. of the vaccine, as well as uncounted millions in the hands of pharmacists and physicians. Secretary Folsom of the Department of Health, Education, and Welfare has blamed "public apathy" for the lag in the program.

Only four states have used up their grants from an original federal fund of $53,600,000 to help states in providing free vaccine to persons under age 20. They are Illinois, Kansas, North Dakota, and Vermont. Two others, Massachusetts and Rhode Island, have used all but a few dollars of their grants.

With this background, PHS Surgeon General Leroy Burney suggested families use the holiday season to arrange for inoculations for all persons under 40 years of age who have not had three injections. "Vaccine protection of unprotected children may mean that some will be around happy and well at future Christmases who otherwise may be crippled or killed by polio. And parents and others under 40 years of age should arrange their own protection. I personally have seen instances in which both parents in an age span between 22 and 25 years have been stricken and one or both crippled for life," Dr. Burney declared.

In another move, the Commerce Department set a quota of 7,000,000 cc. for export of the vaccine in the first three months of 1957. This is the same amount as for the last three months of 1956, and the Commerce Department explained that this high level was being maintained because of the large stocks with the manufacturers.

ANNUITY FOR SELF-EMPLOYED

Weeks in advance of the convening of the 85th Congress, considerable sentiment had been found among the newly elected members for the principle of the Jenkins-Keogh bills. They are the measures that would allow a deferment of taxes on money paid by the self-employed into annuity plans. The American Bar Association's Committee on Retirement Benefits has sounded out House members and found more than half of them in favor of the principle. Of the 435 Republicans and Democrats in the House, 294 were reported in favor, 120 views were unknown, 18 were noncommittal, and only 3 opposed.

Under present plans, a new bill is due to be introduced by Rep. Eugene Keogh (D., N. Y.) that will allow for withdrawal of funds from a retirement plan in advance of age 65 upon payment of a small penalty. The American Medical Association has long supported the Jenkins-Keogh plan because the self-employed are now discriminated against in this field. As early as 1948, the A. M. A. Board of Trustees gave its endorsement of the principle of tax deferment on retirement income.

ARMED FORCES RESIDENCY TRAINING

The Army and Air Force have made separate announcements on their residency training programs. The programs are being given added emphasis in efforts to encourage physicians to enter or remain in the medical services.

The Air Force estimates that since last July 1 a total of 181 of its medical officers have entered residency training in the various medical specialties. Twenty-six are taking training in civilian hospitals, and the rest are assigned to military hospitals. A breakdown of the specialties shows that 33 are taking training in internal medicine; 31 in general surgery; and 20 in obstetrics and gynecology. The Air Force reports that it still has need for more physicians in these specialties and that there are training opportunities also in otolaryngology, pathology, neurology, pediatrics, psychiatry, cardiology, gastroenterology, allergy, and general practice.

The Army is preparing to start its first formal residency training program in preventive medicine next July 1. It will be for a three-year program and is open to Regular Army Medical Corps officers or civilian physicians who accept Regular Army commissions.

Both civilian and military training will be provided over the three years. The first year will consist of an 11-month course in military preventive medicine at the Walter Reed Army Institute of Research, or an equivalent graduate course in preventive medicine or public health at a civilian university.

The second year will be spent in an approved civilian program in a city, county, district, or state health department, and the third year will consist of a formal military residency at a large Army post, with a small portion of the time spent at an Army headquarters under supervision of preventive medicine officers.

Those finishing the full three years will be expected to spend three additional years practicing the specialty to establish eligibility for board examination. For physicians with previous military experience, the military

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From the Washington Office of the American Medical Association.

ARTHRITIS IN THE AGED

L. Maxwell Lockie, M.D.
and
John H. Talbott, M.D., Buffalo

• Because of the many types of arthritis occurring in persons over 60 years of age, therapy must be based on an individual plan suited to that particular person. If the first arthritic attack is severe and in one of the peripheral joints, gouty arthritis should be considered. Here colchicine may be used not only for the initial episode but also in combination with probenecid during the intercritical period. Osteoarthritis, the most common type of arthritis in patients over 60 years of age, may be generally treated with posture exercises, weight control, heat, and aspirin, in addition to individual care. A different form of rheumatoid arthritis may suddenly appear after the age of 60. This condition requires complete bed rest until all activity of the disease ceases. While heat, salicylates, and steroids give relief, gold therapy best seems to stop the progress of the disease. Other forms of arthritic involvement may occur, but, in general, there is a good prognosis for all these conditions.

The challenge of treating the various types of arthritis in patients over 60 years of age is always stimulating. There is so much that can be accomplished that the old saying, "it is your age and nothing can be done about it," does not apply any more. In order to give the greatest relief to the patient, the physician must take time to listen to a detailed history and then to do a careful physical examination. In some instances there are certain laboratory studies and x-rays that are necessary to aid diagnosis and to help in outlining a plan of treatment. Inasmuch as there are different types of arthritis, the correct therapy for each patient must be based on an individual plan suited to that particular person. There are several types of arthritis that are commonly seen after a patient has passed his 60th birthday. These will be discussed under separate headings.

Gout and Gouty Arthritis

If a male has severe acute distress in one of the peripheral joints of the body, the probability that this is gouty arthritis should receive high priority. It is not unusual for the patient to have his first attack when he is past the age of 60. This is one type of disorder of the joints that has significant familial implications. In the majority of patients, it is possible to trace a family history in one or more relatives similarly afflicted. This specific information may be just as helpful in persons in the later decades of life as it is in those in the earlier decades. Approximately 20% of all relatives of gouty patients will have a concentration of uric acid in the serum in the gouty range. However, only a small percentage of these will develop gouty arthritis. An isolated instance of this type of family history is illustrative. In 1940, one of us (J. H. T.) was consulted regarding a 45-year-old man who had had acute attacks of gouty arthritis for more than a decade. His physician noted that this was a case of spontaneous development of gouty arthritis in a member of a family that had no history of the disease. The only living male ancestor was the father, aged 78, who denied any past symptoms suggestive of acute gout. The concentration of uric acid in the serum, however, was in the same range as that of his son, the patient. Three years later, at the age of 81, the father suffered his first attack of gouty arthritis. Two years later, he suffered a second attack.

Significant advances in the understanding of uric acid metabolism have been made during the past decade with the use of isotopes (compounds labeled with radioactive carbon and nitrogen). These investigations have demonstrated the multiplicity of sources of constituents of the uric acid molecule, as well as the many pathways that the various carbon, nitrogen, oxygen, and hydrogen components must travel in order to reach the end-product.

Diagnosis.—The diagnosis of acute gouty arthritis should be presumed upon the clinical evidence and confirmed by laboratory studies. The greatest help in diagnosis, however, is obtained from the clinical characteristics of the acute attack. Sudden onset of acute distress in one of the peripheral joints of the hands or feet of a male points to one diagnosis only. Appearance of the cardinal signs of inflammation—redness, heat, swelling, and pain—in one or more joints of the upper or lower extremities justifies a strong suspicion of gout. The response of acute gout to colchicine, administered orally or intravenously, may be extremely helpful since colchicine is the specific treatment for acute gouty arthritis and has no significant antiarthritic effect in any other type of disease of the joints. Without exception, the other antirheumatic agents that may be given for acute arthritis, such as salicylates, phenylbutazone, and the steroids, are endowed with no diagnostic implications. Relief may follow administration of any of these agents in gouty arthritis as well as in nongouty arthritis. The concentration of uric acid in the serum may also be helpful in diagnosis. Serum or plasma, rather than whole blood, should be used. The patients should have taken no antirheumatic drug within 48 hours of the collection of the blood for the determination of serum urate.

In our clinic, we have found that the patient with gout has a concentration of uric acid in the serum above 6 mg. per 100 cc., irrespective of the stage of the disease and the time in relation to an acute attack. The only agents that modify the concentration are

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From the University of Buffalo School of Medicine and Buffalo General Hospital.

Read in the Symposium on Rehabilitation before the Joint Meeting of the Section on Orthopedic Surgery and the Section on Physical Medicine at the 105th Annual Meeting of the American Medical Association, Chicago, June 14, 1956.

those that lead to an increased excretion of uric acid by the body, that is, the antigout agents other than colchicine. Colchicine has no demonstrable effect upon uric acid metabolism as determined by either the concentration of uric acid in the serum or the isotope studies.

Treatment.—There are several agents that are now available for the management of an acute attack. Reliance should be placed upon colchicine in the initial episode of gouty arthritis because of its diagnostic as well as therapeutic value. A full course of colchicine therapy should be administered by mouth. Also, one-half the full dose of colchicine may be given during a six-hour period together with 800 mg. of phenylbutazone in divided doses. The adrenal steroids have some antiarthritic properties; however, they probably should be used only for patients unable to take other medicaments and not routinely for management of the acute attack. General measures include rest of the affected joint, a soft diet, and an abundance of fluids.

The management of the intercritical period, which encompasses most of the time for all patients with gout, comprises a few drugs and a few prohibitions—in short, a simple schedule. A high fluid intake is to be stressed, because it aids in the elimination of uric acid from the body. Weight-reduction should be insisted upon, if indicated; a low-fat diet is to be used; and substances high in purine, such as liver, kidney, and sweetbreads, should be avoided. Alcohol, in moderation, and red meat are permitted for most patients. The amount of physical activity should be determined by factors other than the presence of gout. It is believed that there are only two drugs that should be used regularly in the intercritical period. These are colchicine, because of its prophylactic properties, and probenecid, because of its uricosuric action. Patients moderately or severely afflicted with gout should take one or two colchicine tablets every day, while those only mildly afflicted probably should take a few colchicine tablets each week. At either dose level, neither gastrointestinal disturbance nor chronic tolerance to colchicine should develop. We believe that the prophylactic use of colchicine is a significant contribution to the management of this disorder.

Probenecid, the second drug indicated in the management of the intercritical period of gout, is a strong uricosuric agent that produces a 20-30% increase in excretion of uric acid in the urine when administered in doses of 0.5 gm. twice daily. A decrease in the concentration of uric acid in the serum occurs with the increased excretion of this substance in the urine. Probenecid has been used at our clinic for more than six years. During this period of time, the favorable results have predominated and the untoward results have been minimal. The prophylactic action of colchicine complements the uricosuric effect of probenecid. This combination is responsible for the present satisfactory status of the management of this type of disease of the joints.

Osteoarthritis

Most people over the age of 60 have some evidence of osteoarthritis as it is manifested by stiffness, pain on motion, or bony enlargement of various joints. The peripheral joints or the spine may be involved. It is usually annoying, not incapacitating, and is the least serious of all types of arthritis. The symptoms are the result of degeneration of the lining of the joints. Frequently spur formation or new bony growth will occur around the margins of the joints. There is no evidence of infection present. The most common age of patients at onset of symptoms is 45 to 60 years. X-ray findings are often helpful but are secondary to the findings on physical examination. When the hands are involved, the arthritis usually occurs in the interphalangeal joints. There will be some enlargement, which is due to capsular thickening, and no free fluid is present inside the joint cavities. When the terminal joints of the hands are involved, the condition is called Heberden's nodes. The onset of symptoms of these nodes at the end joints of the fingers usually occurs within two years of the beginning of menopause. In 10% of these patients the proximal joints will also become painful and stiff.

Diagnosis.—An important diagnostic sign in osteoarthritis of the hands is the fact that the metacarpal-phalangeal joints are never involved. If ever there is pain or swelling in this group of joints, it is due to rheumatoid arthritis. When the joint between the metacarpal bone of the thumb and the adjacent wrist bone is involved, this is always a manifestation of osteoarthritis. The wrist, elbow, and shoulder may be involved, but the discomfort is diffuse and there is full range of motion present in these joints. The cervical spine is frequently affected. On examination, there is limitation of motion or pain on motion. This may remain localized, or the pain may radiate down the arms and even into the hands. Many patients with osteoarthritis will have a history of whiplash injury due to an automobile accident. The examiner should insist that the patient rotate or tilt the neck to a maximum degree to determine the full extent of disability.

The thoracic spine always shows some spur formation on x-rays, but seldom are any symptoms present. However, the lumbar spine frequently is involved. Lumbago in patients over 60 years of age most often is due to osteoarthritis. The poor posture that most people have assumed while watching television or slouching in easy chairs has aggravated many of these symptoms. Here, x-ray studies frequently show marked spur formation, but it must be remembered that it is a well-accepted fact that many people with extensive bony changes in the spine may not have any symptoms of either pain or discomfort. On examination, there is usually no segmental motion present. Muscle spasm may or may not be found. Most often tests of function of lumbosacral joints show little motion, and, when there is motion, the pain brought about by extending the back may be severe. In patients with disability of lumbosacral joints, the physician may frequently obtain a history of a sit-down fall some time previously.

In cases of arthritis of the hip joints, the patient usually is overweight. Rarely are other joints involved. This form of osteoarthritis progresses slowly and may become very disabling. Of all types of arthritis, it is the most resistant to treatment. In the female who is over 60 years of age and overweight, the knees are likely to be the site of osteoarthritis. There will be some bony enlargement, but no fluid is present in the joint cavity. The center of the pain is over the anteromedial aspect of the head of the tibia. Full range of motion is present. X-ray study frequently shows spur formation at the margins of the bones and also some reduction of the joint space due to cartilage destruction. Occasionally the big toe is involved, but the pain here is never localized at the medial aspect as it is in gouty arthritis.

Although x-ray findings cannot always be correlated with symptoms, in the case of osteoarthritis affecting the knees, the greater the changes seen on x-ray, the greater the patient's complaints.

Treatment.—The treatment of osteoarthritis must be individual for the particular patient. However, a general summary of the steps we use in treatment follows. The patient is taken into our confidence and instructed in detail concerning the diagnosis, treatment, and, as far as possible, what to expect in the future. We recommend that undue strain or excessive use of the involved joints be avoided as much as possible. Inasmuch as most patients with osteoarthritis are overweight, reduction of weight at the rate of 1 lb. per week is advised. This is so important that, if the patient with osteoarthritis of the knees does not lose weight, she is not encouraged to return until there has been some weight loss. The infrared heat of either a simple 250-watt bulb or a metallic element frequently gives considerable help. It should be used two or three times a day for 15 minutes each time, at a distance of approximately 30 in. from the skin, at which distance the heat reaching the patient is not uncomfortable.

Since posture is so important in treatment of osteoarthritis, we suggest that the mattress of the patient's bed should be firm. If a rubber or inner-spring mattress is used, a half-inch piece of plywood should be put under the whole mattress. The patient is encouraged to sit only in straight-backed chairs or in occasional chairs, never in a lounge chair or lounge davenport. To keep the patient mindful of good posture, she is encouraged to stand erect with her shoulders back and take six deep breaths every hour on the hour.

We have found that aspirin is usually the best medicament for the relief of pain or stiffness. The injection of steroids in or around involved joints, particularly the thumb, knees, and big toe, will frequently give excellent results. If there is persistence of pain in the cervical area, the use of traction at home is encouraged. In the case of Heberden's nodes, light massage, two minutes to each finger, after heat treatment, seems to help relieve some of the stiffness. If the lumbar area is involved, a lumbosacral support or even a sacroiliac support relieves the strain.

Rheumatoid Arthritis

Patients may show the results of an old rheumatoid arthritis with marked joint changes, but there also may be another variety of rheumatoid arthritis that is seen frequently after the age of 60. This is by no means unusual. Typically, the patient will have had a sudden onset of rapidly spreading rheumatoid arthritis, previous to which he may have been very well. The proximal interphalangeal joints and the ulnar aspect of the wrist show the greatest changes; there is limitation of extension of the elbows, knees, and ankles. Pain, fatigue, and disability may be great. The laboratory studies show an increase, which may be marked, of the sedimentation rate; anemia is present; and there may be some leukocytosis. The x-ray studies are normal, as the arthritis usually has been present only a short time. Of all patients who have rheumatoid arthritis, these people in the older age group do by far the best.

Treatment.—Complete bed rest without weight-bearing at any time is absolutely necessary for as long as any activity of the disease persists. The bed rest must be supervised carefully in order to prevent deformities in the joints, and the mattress must be firm. The patient is allowed to sit up in bed six times a day for 30 minutes each time. Only one pillow is allowed for the head, and another is put inside the bed at the foot, to prevent the bedclothes from pressing on the feet. At no time is a pillow allowed under the knees. As the patient improves, he is permitted to be up gradually. This period of time naturally increases as the patient continues to feel better.

It is our impression that the intramuscular injection of gold is the most powerful treatment to use to stop the progress of rheumatoid arthritis. Our experience goes back some 22 years, during which time approximately 1,000 patients have been treated. Either of two gold preparations, gold sodium thiomalate (Myochrysine) or aurothioglucose (Solganal), is used intramuscularly. The dosage schedule begins with 10 mg. of the gold salt given intramuscularly the first week, 20 mg. the second week, 30 mg. the third week, and 40 mg. the fourth week. Dosage is then kept at a level of 40 mg. given intramuscularly each week until the patient has had a total of over 500 mg. At that time, it is necessary to decide whether to continue administration at weekly intervals, to reduce the dose, or to increase the interval between doses. The decision will depend entirely upon the condition of the patient. There are some reactions that may occur, but these are familiar to all.

Some form of heat is definitely indicated to help relieve the pain in these patients. An infrared lamp, diathermy unit, or baker is soothing and can be used in the hospital; when the patient is at home, the infrared lamp or baker is helpful. If the hands are involved, paraffin baths are soothing. Salicylates, especially in the form of aspirin, are effective to help relieve pain. The adrenal steroids are used in a few selected patients for a short time only in order to make them more comfortable. At no time are they used unless it is deemed absolutely necessary. Many patients have done very well under this general plan of treatment. In most cases, the prognosis is excellent. It may take months to accomplish this, but time is absolutely necessary in this type of treatment: haste does not help.

Other Conditions

Occasionally diabetes and syphilis produce arthritis that becomes manifest after the patient is 60 years of age. In this type of arthritis there is relatively little pain, but often the instability of the joint is marked. When a patient has severe monarticular arthritis that has not responded to treatment for gout or any other type of arthritis, the diagnosis of a malignant growth must be seriously entertained. This type of arthritis is the only one in which it is necessary to give morphine. The condition of Dupuytren's contracture is frequently overlooked, although the disability produced may be great. Therefore, it is wise to examine the palms of a deformed hand as well as the joints themselves. This disability is not to be confused with osteoarthritis or rheumatoid arthritis.

Comment

It is extremely important to make the correct diagnosis of the type of arthritis that is present. A careful examination is necessary in order to plan a proper program of treatment. Fortunately, a high percentage of patients who have arthritis in the over-60 age group can be benefited markedly, with the aid of correct treatment. The prognosis in general is good.

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FRACTURES IN THE AGED

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• *Fractures are an important cause of disability and death in people over 70 years old; they are three times as frequent in women as in men, and more than a third of them are fractures of the hip. The coexistence of other causes of disability must be taken into account in planning surgery, but the elderly patient without serious complicating disease is a good operative risk. Sedation, anesthesia, splinting, casts, fixation, and postoperative exercise should be adapted carefully to the individual case, and sometimes they have a profound effect on the attitude and progress of the patient. In cases of compression fractures of the vertebral bodies, no attempt is made at reduction unless dislocation or facet instability has occurred; the compression is accepted, and excellent results are obtained by a suitable program of physical therapy. The fractured hip, a major problem in the aged, is more successfully treated since the introduction of the three-flanged nail for stabilization. It is important to make use of mechanical aids for early ambulation, to relieve pain, restore weight-bearing, and avoid the complication of stiff joints. Continued, organized help after the patient has gone home from the hospital is frequently essential for complete rehabilitation.*

Fractures in the young and fractures in the aged present specific problems. Fractures in children have received wide attention, but the aged have increased in number in recent years and "have come into their own." These patients must now be dealt with as a separate age group with its own special problems.

Recent surveys of patients hospitalized on the fracture service at the Massachusetts General Hospital reveal that aged persons, patients 70, 80, or 90 years old, constituted 25% of admissions. Females outnumbered the males three to one. In this group, fracture of the hip was the commonest fracture (35%), with Colles' fractures second (16%) and fractures of the neck of the humerus third in frequency (14%). There were relatively few fractures of the femur, the tibial shafts, or the ankle. The over-all mortality rate for the aged patients on our fracture service in 1955 was 10%. The mortality rate for those with intertrochanteric fractures was 18% and for those with fractures of the femoral neck 10%. In 57 major operations on elderly persons during the past year, 8% of the "good-risk" and 20% of the "poor-risk" patients died as a result of surgery.

Characteristics of the Aged Patient

Fractures occurring in the elderly person may be complicated by hypertension, some degree of cardiac failure, respiratory complications, malignancy, or metabolic, renal, and nutritional diseases. These may occur at any age, but are found more frequently in the aged patient. Contrary to general opinion, however, the aged patient without serious complicating conditions is found to be a very good operative risk. We agree with Moyer and Keyes [1] that the aged patient should not be denied necessary surgery or specific therapy merely on the basis of "old age," that the "magnitude of the operation is not as important a determinant of operative risk among the aged as is the duration of the period of physiological upset attending it." We have found that the aged patient does not tolerate the added stress of such prolonged complications as cerebral accident, recurrent phlebitis, sepsis, or diabetes.

In one respect the aged are much like children; they need good, constant, intelligent nursing care. In the early phase of treatment for major fractures, they must be made comfortable and turned frequently to prevent pulmonary stasis, pressure sores, urinary stasis, and fecal impaction. Constant pain and immobilization are extremely exhausting to the aged. Restraints and narcotics add to mental confusion and restlessness; when these are eliminated the patient may become more cooperative and quieter. Aspirin in adequate doses and codeine in small doses should control the average discomfort and may be far more effective than strong narcotics. Chlorpromazine in selected cases has proved very effective in relaxing elderly patients and lessening

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Read in the Symposium on Rehabilitation before the Joint Meeting of the Section on Orthopedic Surgery and the Section on Physical Medicine at the 105th Annual Meeting of the American Medical Association, Chicago, June 14, 1956.

pain. Care, patience, and guidance are needed when the aged patient is taught to walk, because the elderly person may lose his balance easily. Many are discharged to their homes or to a nursing home on crutches, in a plaster cast, or for "bed and chair existence." Much that is gained in the hospital can be lost after discharge by neglect of the patient, mishandling of the extremity, or noncompletion of specific activities and exercises.

Bone Condition.—The bone picture of an aged person reflects his general condition (fig. 1). There are "young," resilient individuals in the 80's whose bone structure may vary little from that of the average adult. On the other hand, there are "old" individuals in the 60's with far-advanced osteoporotic changes. Osteoporotic bone of old age is not "decalcified." In analysis, i. e., grain for grain, the calcium content in osteoporotic bone and normal bone is the same. Rather, there is an actual loss of bone substance or mass. The bone trabeculae are thinner and fewer than normal. The causative factors of osteoporosis in old age are the lack of sex hormones, malnutrition, inactivity, and the aging of tissues.

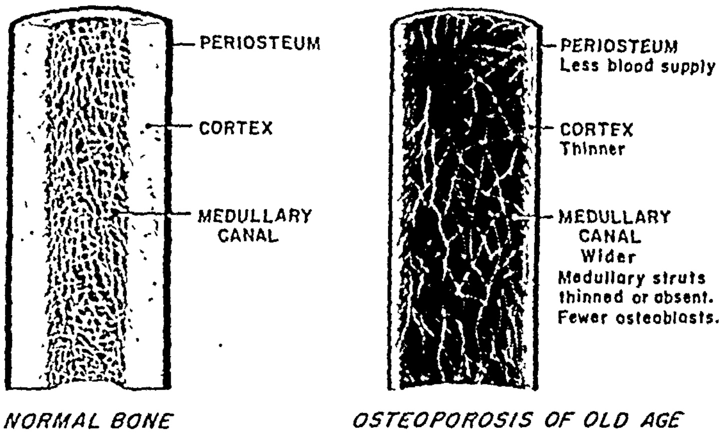
PERIOSTEUM
CORTEX
MEDULLARY CANAL
PERIOSTEUM Less blood supply
CORTEX Thinner
MEDULLARY CANAL Wider Medullary struts thinned or absent. Fewer osteoblasts.
NORMAL BONE
OSTEOPOROSIS OF OLD AGE

Fig. 1.—Schematic comparison of normal bone and that showing osteorosis that occurs in old age. This condition is caused by lack of sex ormones, malnutrition, inactivity, and aging of tissues.

Due to the loss of bone substance in osteoporosis,[1A] the bone is weaker and more brittle in the aged patient than in a younger individual. The bone heals more slowly, due to the smaller amount of bone equipment—bone substance, osteoblasts, blood clots, and muscle coverage—needed to initiate a good callus. The thin bone cortex and large, poorly filled medullary canal present a definite mechanical problem for early activation and ambulation. Internal fixation, such as plates and screws, is poorly tolerated, so careful evaluation of the patient and the x-ray films is necessary in order to determine whether the bone is strong enough to tolerate internal fixation. Little is gained (in fact, harm may be done) when internal fixation is applied to bone too weak to accept it. In recent years, procedures for intramedullary fixation have been tried in osteoporotic bone. These have been encouraging in selected cases and in experienced hands. Estrogens to stimulate osteoblastic activity, or testosterone to stimulate growth of muscle mass and appetite, and a high-protein diet are useful adjuncts in therapy. Extra calcium itself is not needed; in some instances it may be harmful.

Anesthesia

Careful evaluation of the patient before anesthesia is most important in the aged. We suggest that the preoperative procedures include determination of the patient's hemoglobin level and nonprotein nitrogen level, urinalysis, and taking of an electrocardiogram and chest x-rays. Beecher[2] makes the following suggestions for anesthesia in the aged patient. Relative to major surgery he suggests, "Almost any anesthesia to which the anesthetist is accustomed is good choice for hip fractures in good-risk patients. In poor-risk patients, with anesthetists of varied skill, our patients seem to do best with a combination of nitrous oxide and ether, the ether being used to provide relaxation only when needed." Beecher also says, of preoperative medication, "Minimal doses of sedatives and atropine are wise in pre- and post-operative medication. We like pentobarbital sodium 0.1 gram, intramuscularly with atropine 0.6 mgm. sc."

Reduction of a large number of forearm fractures, particularly Colles' fractures, has been done in our hospital with the use of brachial block anesthesia. This anesthesia allows manipulation of the fracture regardless of when the patient has eaten. There have been 687 brachial blocks performed at the Massachusetts General Hospital, with a 2% incidence of reported pneumothorax. However, Beecher says, "we suspect minor degrees of pneumothorax to occur at a greater incidence." Only one death could be attributed to this complication, so we assume that it is a safe type of anesthesia for aged patients. Against this mortality rate can be balanced that of general anesthesia, a death rate of 1 in 800. Practice in the performance of brachial block is especially important in avoiding complications. Multiple nerve blocks around elbow and ankle joints have been very successful, using a 1% solution of lidocaine (Xylocaine) hydrochloride with epinephrine. The anesthetic effect is prolonged by the addition of epinephrine. Spinal anesthesia is not used in poor-risk patients or in instances of shock or impending shock in the elderly patient.

Fractures of the Upper Extremity

The primary aim in treating fractures of the upper extremity in aged patients is to restore a useful hand, in those of the lower extremity to enable the limbs to bear weight. Fractures of the upper extremity in the aged as a rule heal readily. The disturbing complications are stiff, painful fingers or limited motion in the wrist, elbow, or shoulder. These complications may persist long after the fracture has healed and may become a permanent partial disability.

Colles' Fractures.—In Colles' fractures a gentle reduction is performed with the application of a light, removable "gutter" splint or a plaster cast allowing free motion and use of the fingers. Immediate elevation of the hand after manipulation is very important. If early edema is prevented from occurring, the vicious cycle of edema, pain, and stiffness is eliminated. If the Cotton-Loder position is used, the wrist should be brought to a more neutral functional position as soon as possible. The patient should begin careful elbow motion and shoulder exercises as soon after reduction of the fracture as this can be comfortably performed. Early, clear instruction in this is most important. The same principles apply to fracture of the forearm.

Fractures of Elbow.—In comminuted fractures of the elbow, a light plaster splint is applied with the elbow in a stable position—preferably extended a little beyond a right angle. Finger and shoulder motion should be started early. In displaced fractures of the olecranon, we have had gratifying results by resecting the proximal fragment and suturing the triceps to and over the ulna or distal part of the olecranon. Motion is begun within a week. The functional and cosmetic results have been excellent. This form of treatment eliminates immobilization.

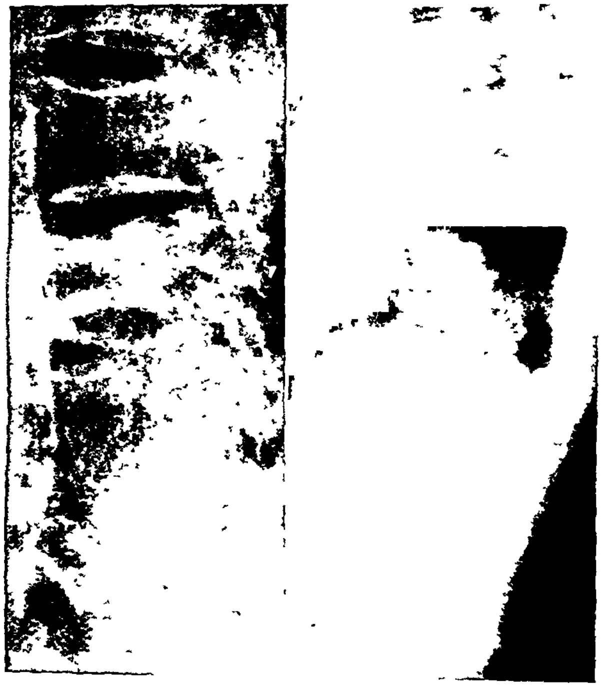

Fig. 2.—Compression fractures of the vertebral bodies in aged patients with osteoporosis. *Left*, roentgenogram of a 79-year-old man who suffered a compression fracture of the first lumbar vertebra from a fall. *Right*, roentgenogram of an 85-year-old woman, showing compression of the fourth lumbar body.

Fractures of Humerus and Shoulder.—In fractures of the humerus, we favor conservative closed methods of treatment with light-weight coaptation splints with the arm at the side or a light-weight hanging cast. In fractures of the shoulder, the patient is made comfortable with a sling and swathe, an axillary pad, and the arm at the side. An anatomic reduction is not a prerequisite to good function, and, as a rule, repeated manipulation or open reduction is not necessary. Shoulder motion is started early, the swathe is removed as soon as possible, and normal activities of the arm are begun within the limits of comfort.

Fractures of Spine.—The aged patient with a "broken back" is a very different problem from the young adult or middle-aged patient with this condition. Elderly patients, particularly females, may develop rather severe osteoporosis, especially in the vertebral bodies. This is commonly referred to as postmenopausal osteoporosis. Compression fractures of the vertebral bodies may be produced from slight strain or merely a jolt (fig. 2). As a rule, no attempt is made to reduce the vertebral fracture in the elderly patient unless dislocation or facet instability has occurred. The compression is accepted, the patient is allowed to assume comfortable positions in bed, and hot packs and mild analgesics are used. The patient is encouraged to walk as soon as the pain subsides, which is usually within a two-week to three-week period. The clinical results with this program have been excellent. When reduction is attempted, the fracture usually returns to its original deformity when the patient becomes ambulant. Attempted reduction of fractures of vertebral bodies in the aged may also invite serious complications.

Following is an outline of suggested treatment: Plaster casts are rarely used, and hyperextension is not used to reduce the fracture. We advise bed rest, with hot packs applied four times a day for 20 minutes until pain has subsided, and administration of enteric-coated aspirin (0.6 gm.) four times a day. A high-protein diet is recommended, in addition to therapy with testosterone or estrogen in selected cases. Muscle-setting exercises should begin early, as should ambulation, with the patient wearing a well-fitted corset.

Fractures of the Lower Extremity

The fractured hip is the major problem in the aged patient. Bigelow,[1] in 1869, wrote, "The prognosis of these fractures is difficult to give. Elderly people may die of them at the end of a few weeks, or may linger many months." Much has been accomplished since that time. When Smith-Petersen, Cave, and Van Gorder[4] reported their results using the three-flanged nail to stabilize fractures of the hip in 1931, the management of fractures of the femoral neck was put on a safe and reasonable basis. Stabilizing the fracture

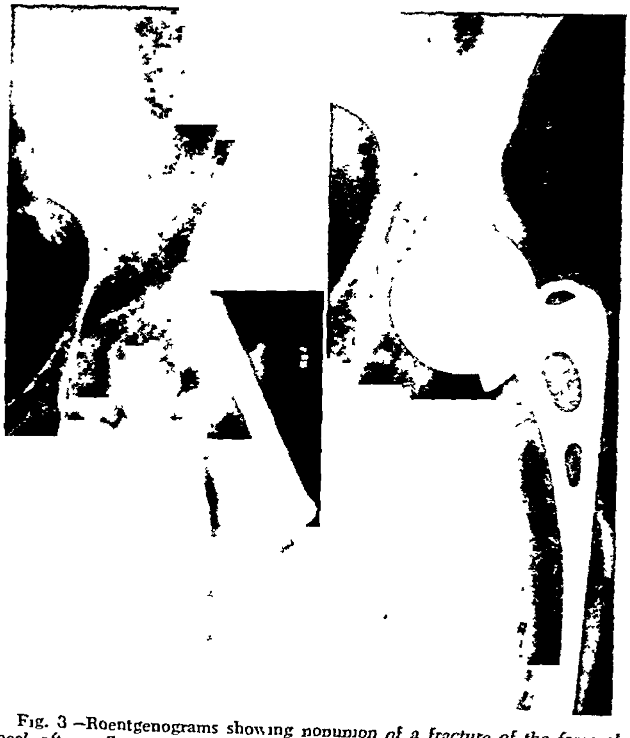

Fig. 3—Roentgenograms showing nonunion of a fracture of the femoral neck after nailing in a 75-year-old woman. *Left*, nonunion of neck of left femur. *Right*, insertion of a Moore-type Vitallium prosthesis.

relieved pain and allowed the patient to be turned and to be made ambulant within a reasonable length of time.

Since then, many types of appliances have been used to stabilize fractures of the femoral neck. In recent years, replacement prostheses of various types have been used in fresh fractures of the femoral neck that could not be satisfactorily reduced or in the very old patient who would have to be made ambulant within a few days of surgery. The technique of introducing the prosthesis in the aged person must be adapted to osteoporotic bone. When the replacement prosthesis is used in selected cases and by experienced surgeons, the results have been very good. In inexperienced hands, some very distressing complications have occurred.

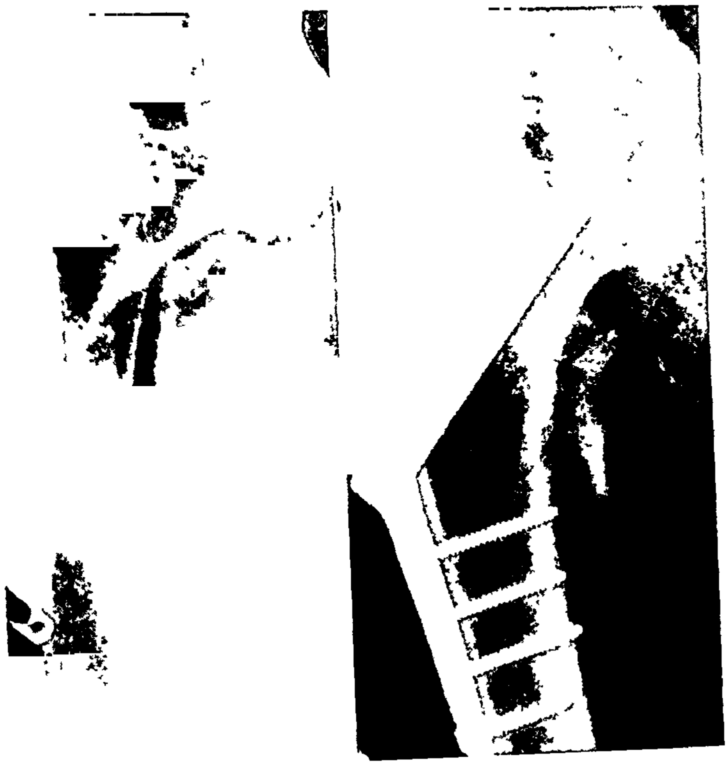

Fig. 4.—Roentgenograms showing an intertrochanteric fracture suitable for internal fixation in a 75-year-old woman. *Left*, intertrochanteric fracture with little comminution and strong fragments. *Right*, internal fixation with a Jewett nail-plate combination.

There is general agreement today that nonunion of the neck of the femur occurs in approximately 20 to 25% of fresh fractures of the femoral neck that have been nailed. Aseptic necrosis develops in 60% of those with nonunion of the femoral neck.[3] The replacement prosthesis has been a definite help in allowing the patient to recover from these complications and to become active in a relatively short time (fig. 3). Other reconstructive operations, such as the geometric osteotomy of Dickson, the Colonna procedure, or shaft arthroplasty, using a Vitallium mold, can be very successfully employed. Impacted fractures of the neck of the femur in valgus position, with good anteroposterior and lateral roentgenograms, are stable in a high percentage of cases and may be treated satisfactorily without operation. Some surgeons prefer to nail or introduce a screw for fixation in these fractures.

Intertrochanteric fractures occur in an older age group than fractures of the femoral neck. Stable fractures can be treated without operation, but six to eight weeks are necessary before ambulation is safe. The decision for open reduction and internal fixation with a nail-plate combination depends upon the quality of the bone and the degree of comminution Badly comminuted fractures with marked osteoporosis may respond poorly to open reduction; in fact, harm may be done by introducing some form of internal fixation. The fragments are too brittle to be held by nail and plate combinations. However, when the quality of the bone is good and the fractured fragments are strong, a nail-plate combination will prove very effective (fig. 4).

Fractures of Femoral Shaft.—Fractures of the femoral shaft in the aged are serious. Some patients are physically able to tolerate traction and suspension, whereas others become mentally confused by enforced immobilization and confinement to bed. This reaction seems more severe in patients with fractures of the femoral shaft than in those with fractures of the hip In a large percentage of patients, the bone structure of the femur is too osteoporotic to tolerate "onlay fixation," such as plate and screws.

Intramedullary fixation of fractures of the femoral shaft in the aged patient has been a distinct advance. There are many technical problems, such as the thin cortex of the femoral shaft and large medullary space. We have used the largest Küntscher nail (11 or 12 mm.) or a "nesting" of nails (2/12-mm. nails) to obtain good internal fixation. Parham bands around comminuted fracture fragments aid greatly in stabilizing the fracture site. An intramedullary rod will eliminate pain and allow motion and nourishment of the patient.

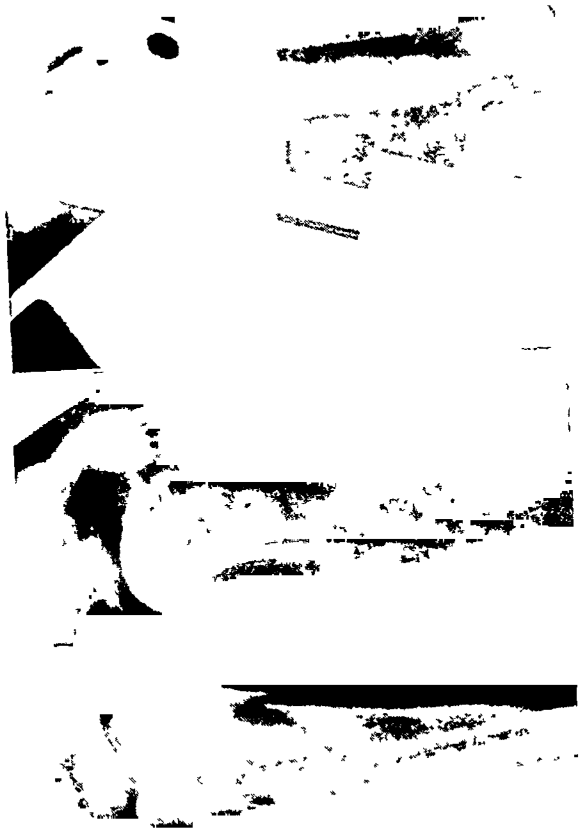

Fig. 5.—Treatment of a 73-year-old woman with a comminuted fracture of the femoral shaft above the condyle on a Bohler frame, with traction through the tibial tubercle. Roentgenograms showing, *top*, traction and suspension with a wire through the tibial tubercle, *center*, consolidation of the fracture at the time of ambulation, and *bottom*, consolidation 10 weeks after injury.

Many patients can be in a chair or walker in a relatively short time. A confused elderly patient whose condition is deteriorating changes within a few days to a clear-minded, cooperative, happy individual. A word of warning is necessary. Intramedullary fixation calls for experienced surgeons, proper instruments, and adequate help. Unless these are available, this form of surgery should not be attempted.

Fractures of the Femoral Condyle.—Elderly patients tolerate fractures of the femoral condyle much better than they do fractures of the femoral shaft or even those of the femoral neck. It is surprising how well they do after treatment with a pin or Kirschner wire through the tibial tubercle, with balanced traction and early motion of the knee (fig. 5). Open reduction, using a Blount nail or plate, is indicated in some instances. However, the bone must be strong enough to tolerate the stabilizing equipment. In figure 6, a poor selection of a case for internal fixation is shown. Although good reduction was obtained, the bone was too porous to retain the apparatus.

Pathological Fractures

The possibility of metastatic disease should be considered in any elderly patient with fracture of a long bone, particularly a fracture of the humerus or femoral shaft. A chest roentgenogram should be taken routinely, and a skeletal survey completed if necessary.

Intramedullary fixation is frequently indicated in pathological fractures, expecially in those involving the lower extremities. Pain is relieved, and the patient may walk and return home in comfort within a relatively short time. Death usually intervenes before the local area is affected to any extent by tumor growth.

In fractures of the femur due to osteitis deformans (Paget's disease), intramedullary fixation has proved very effective for early ambulation of the patient. It has been necessary to perform an osteotomy on the shaft above or below the fracture site, in order to introduce the rod. The patients actually appreciate having their legs straightened, and several have stated that they were waiting to break their other femur "in order to have two straight legs"! Figure 7 illustrates the remodeling and change in stress lines following introduction of a Küntscher rod for a fracture of the femoral shaft due to osteitis deformans.

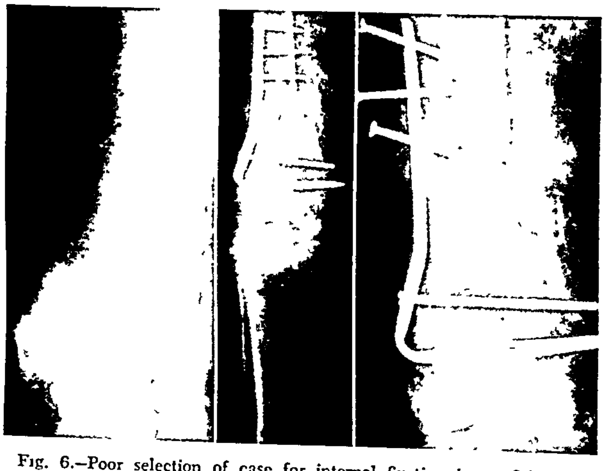

Fig. 6.—Poor selection of case for internal fixation in an 85-year-old woman. Roentgenograms showing, *left*, a displaced supracondylar fracture of the femur, *center*, good reduction with a Blount plate and screws, and, *right*, plate and screws not held by weak osteoporotic bone.

Need for Long-Term Care

Much progress has been made in the treatment of fractures in aged patients during their period of hospitalization. This has come about through the combined efforts of the surgeon, physician, nursing service, anesthesia service, and physical therapy department. Social service has been of inestimable service in individual cases but is limited in the over-all picture. Organized efforts in the care of the aged patient fall off abruptly, however, when the patient is discharged from the hospital. The average mother taking care of her home and her children is not able to give the necessary time and care to a grandmother recovering from a broken hip. The average nursing home lacks the trained personnel and equipment for adequate care and rehabilitation of the aged patient. There is an urgent need at the present time for organized long-term care and supervision of the injured aged patient during the period of recovery after hospitalization. This help should come from local, state, and federal governments and should be patterned after the state crippled children's program. The problem of the injured aged patient is with us at the present time. There is every indication that it will continue to grow.

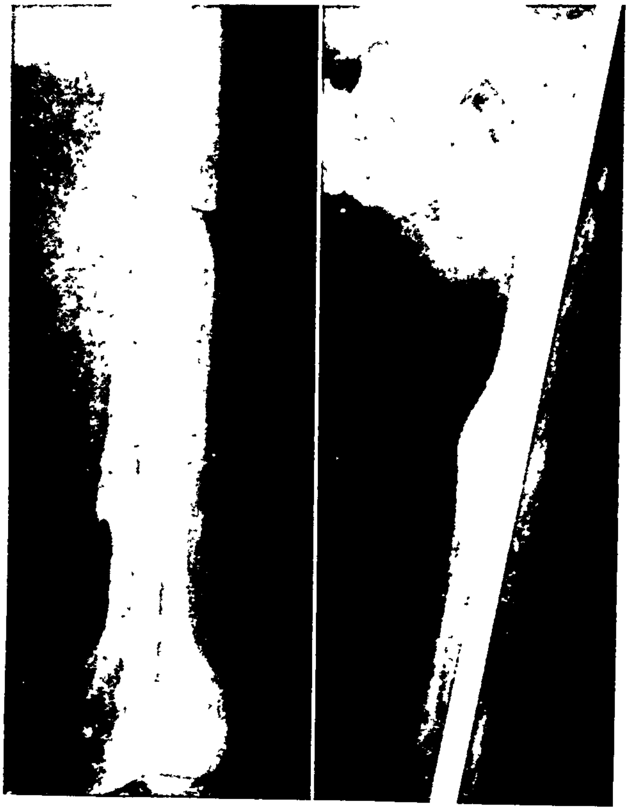

Fig. 7.—Roentgenograms showing intramedullary nail (11 mm. in diameter) used for stabilization of a femoral fracture in an 84-year-old man with osteitis deformans (Paget's disease). *Left*, fracture through the lower third of the femur. It was necessary to perform osteotomy on the femur above the fracture in order to introduce the straight nail. *Right*, improvement in cortex one year later after intramedullary fixation.

Summary

With the increase in longevity, and better care of the hospitalized patient, aged persons in the population have become a gradually enlarging group with specific problems of their own. One of these problems is the unique treatment of fractures necessary in this age group. As a rule, fractures of the upper extremity in the aged patient can be treated with good results, as these do not confine the elderly patient to bed; the primary concern is to avoid the complications of painful, stiff joints. In fractures of the lower extremity, mechanical aids frequently must be used in order to permit early ambulation. The primary aim is to relieve pain and restore weight-bearing. Specific attention must be given to the general condition of the patient and the degree of osteoporosis present.

Much progress has been made in care of aged patients during their hospital stay. However, comparatively little progress has been made in their care during the period of recovery after hospitalization. There is an urgent need for organized help to the aged patients after their discharge from the hospital.

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MENTAL REACTION TO TRAUMA AND HOSPITALIZATION IN THE AGED

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• *The removal of an elderly person to a hospital during acute illness or after an injury involves certain difficulties and dangers that need to be recognized. Disorientation leads sometimes to delirium, which in severe cases can exhaust the patient. Many simple steps can be taken to aid the patient in keeping oriented, such as having a member of the family at hand, leaving a night light on, and avoiding sedatives that may increase the patient's confusion. The presence of familiar objects and the observance of familiar rituals such as a nightly drink of brandy have excellent sedative effects. Early ambulation and occupational therapy are important. If such measures fail and delirium becomes dangerously severe, the patient should be transferred to a psychiatric ward or hospital for special care.*

The behavior of elderly people frequently, and perhaps unfairly, is compared to that of children. However, many parallel patterns do exist in the sphere of emotional reactions to trauma and hospitalization. The child reacts in an apprehensive, confused, and sometimes terrified manner to an injury and sudden transfer from a familiar environment to strange hospital surroundings. The organization of his personality is as yet insufficient to integrate these changes, and the consequent anxiety is frequently overwhelming. These reactions are intensified during the night, when the semidarkness and shadowy figures give full rein to the child's fantasies and imagination. It is often amazing how a child's anxiety can be ameliorated by the presence of a familiar person or a familiar toy from home. These serve as ties between the child and home, thus diluting the separation and ensuing strangeness.

Many of the same reactions are seen in aged persons after trauma and hospitalization. The single most constant symptom in elderly persons under such circumstances is that of delirium, which, as in the child, is greatly intensified at night. The delirium is characterized by complete disorientation for time, place, and person; some degree of agitation and panic frequently is apparent, and, in the more severe forms, destructiveness and incontinence appear. Depending on various individual factors, the patient may exhibit hallucinations, paranoid delusions, or combativeness and literally may exhaust himself. The delirium often may be far more dangerous than the original trauma for which the patient was hospitalized. Again, as with the child, relatively simple measures, such as the presence of a familiar person or illumination from a night light, may prevent the appearance of delirium. Such measures allow the elderly patient to orient himself and remain oriented, which is so difficult in the face of an impaired memory for recent events.

Cause of Disturbed Behavior

Many observers have assumed that this disturbed behavior in old age is purely the result of organic pathological-anatomic brain changes. This automatically implies that the disturbance is irreversible, which in turn leads to a fatalistic approach that is not justifiable in view of the excellent results sometimes obtained by thorough and vigorous treatment.[1] Autopsy findings have shown that many older persons who have never had disturbed behavior and who were quite clear mentally have far-advanced senile and arteriosclerotic cerebral changes. Conversely, many of those who have exhibited disturbed and confused behavior have little, if any, cerebral damage.[2]

The question remains as to what does account for the disturbed behavior so often seen in older persons, particularly after trauma and hospitalization. In large measure, the answer is to be found in the premorbid personality and in the youth of the person in ques-

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Read in the Symposium on Rehabilitation before the Joint Meeting of the Section on Orthopedic Surgery and the Section on Physical *Medicine* at the 105th Annual Meeting of the American Medical Association, *Chicago*, June 14, 1956.

tion, namely, the psychological deficits and conflicts that he carries with him into the increasing pressures of advancing age. Part of the aging process is diminution of resiliency and flexibility and a lessening capacity to adapt to change or stress. The more deficient, immature, or neurotic are the psychological adaptations of earlier years, the smaller is the stress required in old age to produce disorganized or disturbed behavior. Thus, minimal cortical damage is catastrophic to one person and relatively unnoticed in another.[3] Elasticity of the cerebral arteries, although extremely important, is not the only factor; equally significant is elasticity of the personality, as characterized by the ability to adjust to earlier stresses.

Hospitalization

It is obvious that in many cases there is no choice regarding hospitalization of an aged person after trauma. Surgical and orthopedic procedures often must be carried out, and these can be done only in the hospital. In these instances, it is well to be aware of some general principles that may be helpful in warding off serious senile delirium. I shall refer to these principles later. However, in many instances hospitalization has actually been quite harmful and perhaps was the cause of death. This is indeed paradoxical, in that hospitals have as their main and perhaps sole function the relief of suffering and prolongation of life. Report of an illustrative case may be appropriate.

A 79-year-old man had been retired from active business for 11 years and was in remarkably good health. He lived alone with his wife in a small home in which they had resided for the previous 23 years. The patient was fairly alert, except for some forgetfulness and a slight decline in the quality of his personal habits. In January, 1954, while doing some woodworking around the home, he struck his head on a beam. It is not known whether he lost consciousness, but his wife noted that he was somewhat incoherent in his speech. A small hematoma was noted in the right temporal area of the scalp. He was brought to the hospital emergency room, where a careful neurological examination was done and roentgenograms of the head were obtained. Results of the examination were negative, except for mild disorientation and mild impairment of recent memory. It was considered that the patient should be observed in the hospital for 24 hours.

He was slightly restless and mildly confused that evening, but he soon fell asleep after a bedtime dose of 1½ grains (0.1 gm.) of a fast-acting barbiturate. After he had been asleep for about two hours, the nurse heard him calling loudly. When she entered the room, she noted he had a very frightened expression and was calling for his wife and for his son, who had been killed in World War II. He was completely disoriented in all spheres, confused, agitated, and obviously frightened. He was negativistic and refused any medication, thinking that it was poison. It was necessary literally to carry him back to bed and restrain his arms and legs. He was given two hypodermic injections of barbiturates, which appeared to increase his restlessness. He called out all night and struggled against his restraints.

The next morning he appeared ill. He was dehydrated, incontinent of urine, and exhausted. Neurological findings of a focal nature were absent. The psychiatric consultant considered that the patient's condition was not directly related to the head trauma but most likely was a nocturnal delirium aggravated by barbiturates. The patient's wife and daughter stayed with him that day, they fed him and reassured him repeatedly concerning his condition and hospitalization. He was given fluids and vitamins intravenously, and at bedtime he was given his usual brandy. His daughter sat up in his room during the night, and a light was left on. Sedation was not given, and he slept well. When he awakened during the night, his daughter would speak to him and he would quickly drift off to sleep again.

The following morning, the patient was back to normal. He was oriented, calm, and cooperative. The only residual effect was amnesia for the night before and the feeling he had experienced a nightmare. He was dismissed after a neurological recheck examination gave negative results.

Fortunately, this case had a happy ending. The main injury suffered by this patient was not from the blow on his head but from his hospitalization. A period of observation was definitely indicated in this case, but the question remains as to where such observation should be carried out. The answer would appear to be the home, if this is at all possible. Admittedly, this plan is far from ideal in many cases, but the benefits derived from the avoidance of delirium or a state of confusion far outweigh the disadvantages of such an arrangement. In some instances, such delirium and ensuing exhaustion have progressed to the point where electroshock therapy becomes necessary literally as a lifesaving device. In studies regarding nocturnal delirium in the aged, Cameron[4] found that darkness of the room, combined with impairment of recent memory, results in disorientation. Because of loss of retentive powers, the patient is unable to maintain a spatial image without repeated visualization. This disorientation leads to misinterpretation of the environment and lays the foundation for full-blown delirium.

Thus, a primary decision to be made by the physician is the desirability of hospitalization of elderly persons. It is to be remembered that the trauma itself is a serious stress on the elderly patient's ability to make the necessary adjustments. Physical trauma also becomes a mental trauma when the elderly patient foresees a period of helplessness and further dependency, loss of self-esteem, and financial burden. It is easy to see how trauma, with all its physical, emotional, and social implications, can precipitate profound neurotic or psychotic reactions in an elderly person whose capacities are already seriously taxed by the mere act of existing in a society geared to a large extent to the needs of the young and healthy. To add the necessity for the further adjustment to a strange hospital routine is sometimes asking too much.

Although delirium is the most common mental reaction to trauma and hospitalization in the aged, it is by no means the only one. Depressive reactions, either agitated or retarded, are frequent. Also, acceleration of a mild senile dementia may occur or a caricature of a preexisting neurotic reaction may be presented.

Prophylactic Measures

A number of measures can be helpful in avoiding mental complications after trauma in the aged when there is no alternative to hospitalization. Relatives should be asked regarding any special habits or rituals the patient may have; these should be continued providing they do not interfere seriously with hospital routine. For example, an elderly woman who was accustomed to having two glasses of hot lemonade every morning was greatly relieved when she was assured this routine could continue in the hospital. Patient, careful, simple explanations regarding his injury or illness and hospitalization are also helpful to the aged person. The physician must remember that the attention span and recent memory of such patients are often impaired and that repetition is essential.

The prodromal symptoms of an impending delirium or a state of confusion must be watched for. It is relatively easy to recognize such signs, which include restlessness and irritability, easy mental fatigability, mild confusion and disorientation, and increased loss of recent memory. If a surgical procedure is contemplated, it should be postponed when these prodromal symptoms appear. A member of the family should be enlisted to stay with the patient, and a light should be left on at night. With the appearance of restlessness, there is a tendency to prescribe sedatives and narcotics. Many geriatricians unyieldingly forbid the use of barbiturates and bromides in the aged patient. There is a tendency toward excitement or depression of vital functions because of the cumulative effect of these drugs. A good general rule is to give as few doses and as small amounts of medication as possible. Whisky or brandy in eggnog is an excellent nightly sedative in some instances. Brandy has been called the "milk of the aged," and the danger of alcoholism at this period is negligible.[5] Judicious use of the newer tranquilizing drugs, especially chlorpromazine, has been extremely successful in eliminating the need for sedatives and reducing agitation and anxiety.

Ambulation as early as possible is beneficial not only for medical reasons but also for the mental improvement to be derived from the patient's being less restricted in activities and being able to make more social contacts. Such adjuncts as occupational therapy should be employed.

Unfortunately, despite following of the best medical and psychiatric principles, delirium may occur in a significant number of elderly patients. If the delirium is severe, with danger of exhaustion and even death, the patient should be transferred to a psychiatric ward or hospital.

Summary

As patients grow older, the stress of physical trauma and hospitalization may often precipitate a serious mental disorder when the capacities for adjustment are already overtaxed. These psychiatric complications may be far more dangerous than the original reason for hospitalization. If at all possible, observation and treatment of the aged should be carried out at home and hospitalization should be avoided. The commonest and most dangerous psychiatric complication is senile delirium. Although this complication cannot always be avoided, some relatively simple measures and avoidance of overmedication can greatly reduce the frequency of its occurrence.

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PHYSICAL MEASURES IN THE AGED

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• *Two physical aspects of disability in the aged have been especially studied, namely, the inefficiency of respiration and the inadequacy of ambulation. Habitual underventilation of the lungs was suspected in some patients because their vital capacity increased so promptly and so greatly after a program of breathing exercises and because this was accompanied by so marked an improvement of general condition and attitude. Similar evidence led to the conviction that the early achievement of ambulation in the elderly patient is more important than the concentrated exercising of particular groups of weakened muscles.*

The various techniques of physical medicine and rehabilitation in the treatment of specific clinical syndromes in the elderly patient have been well documented.[1] The purposes of this paper are to call attention to the disturbances in bodily functions produced by acute and chronic hypoxia, to demonstrate the need for including in the rehabilitation program measures to improve the efficiency of external respiration when disturbances exist, and to emphasize the necessity for early attempts at ambulation.

Certain changes in bodily function have traditionally been associated with the "normal" process of aging.[2] Among these are pupillary changes, with miosis and sluggish reflex responses to light and distance; changes in ocular movements, with progressive restriction in the movements of convergence and defects in upward gaze; generalized muscular wasting; tremors on effort; elevation of the thresholds for perception of the stimuli of light touch, vibration, and pain; other reflex changes, with loss of superficial reflexes and diminution or loss of the ankle jerk; impairment of the drive to accomplish normal activities; and diminution in strength together with sharp limitations of endurance.

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Read in the Symposium on Rehabilitation before the Joint Meeting of the Section on Orthopedic Surgery and the Section on Physical Medicine at the 105th Annual Meeting of the American Medical Association, Chicago, June 14, 1956.

Perhaps because much of society functions by means of machines of one type or other, we have tended to regard our own bodies as machines. The aging process in various body tissues has been compared to the wearing out of component parts of the machine. That this concept is incorrect may be demonstrated in a number of ways. Changes have been described in neural tissue in the aged that are interpreted not as degenerative processes but as processes of an essentially defensive nature that place the cell in a better position to withstand the metabolic vicissitudes of old age.[3] Work with isotopes has revealed an unexpectedly rapid turnover of protoplasmic constituents in neural tissue at all ages.[4] For these reasons the neuron should be regarded not as a stable system but rather as a system in which there is a steady flow of productive activities. However, there may be degenerative changes within the nervous system that lead to decreased functional abilities and eventually to the death and disappearance of many cells. The difficulty apparently is in the correlation of the functional with the organic changes. Since there is agreement that the changes that modify function precede the final organic changes in the course of the so-called aging process, any therapeutic program might well include consideration of those factors that modify function, in addition to the more easily demonstrable organic factors.

Hypoxia

Whatever else the elderly patient may complain of, fatigue and lack of endurance are extremely common. It has been pointed out that the capacity for work and the fatigue induced by it are related to the intensity and duration of the work.[5] At the one extreme is a 50-yd. dash, which may last five seconds; at the other extreme is a day's labor in heavy industry, which may last as long as 12 hours. In the first example, the work is accomplished by the scanty reserves of oxygen in the body together with the body's resources of anaerobic energy. In the second, the work performed is chiefly on an aerobic basis. Obviously, most daily activities fall into the latter category. The body tissues vary considerably in their susceptibility to hypoxia.[6] The frontal lobes of the brain, for example, are more readily damaged by hypoxia than the rest of the brain cortex or other parts of the central nervous system. The small pyramidal cells of the cortex are more sensitive than the cellular components of the medulla or the spinal cord. The myocardium is the tissue next most sensitive to oxygen deficiency. The permeability of the pulmonary capillaries, and therefore gaseous exchange in the lungs and the function of the adrenal glands, is also influenced by hypoxia. On the basis of these observations, hypoxia certainly can be considered among those changes that may modify function. It remains to demonstrate that a basis for hypoxia exists in the problems encountered in the physical rehabilitation of the aged.

It has long been known that the vital capacity is approximately 10% less with the patient in the supine position than in the erect position and that there is a reduction in vital capacity with age.[7] There seem to be few studies dealing with the magnitude of changes in vital capacity in the older person and more specifically in the elderly patient who has a physical infirmity that we frequently attempt to modify with rehabilitation procedures.

Although clinically one can see a lag in the hemithoracic movements in the patient with hemiplegia, the shallow upper chest respiration in the individual with pulmonary emphysema, and gross disturbances in pulmonary mechanics in other conditions, it is easy to measure vital capacity with acceptable accuracy and thus provide objectivity for such impressions. While vital capacity is not a valid criterion for the degree of efficiency of pulmonary function under all conditions, such measurements do provide a means for observing the progress of a patient over a period of time as well as for comparison of the patient's capacity with normal values.

We have employed the Bennett respiration ventilation meter[8] not only to check the vital capacity of the elderly patient but also to determine the minute volume of respiration for normal quiet breathing. The percentage of the predicted normal attained by the patient with respiratory difficulties may be determined by comparison of the findings for that patient with standard vital capacity tables. The resting minute volume, rather than maximal breathing capacity, was selected because this figure was considered to be a more satisfactory reference base for the respiratory demands of functional activities.

The results of these studies to date indicate that normal vital capacity and minute volume values occur very seldom in the ill older person. None of the patients tested had a vital capacity of more than 70% of the predicted normal; the majority had capacities below 50% of normal. The resting minute volume was reduced in many patients but usually approached normal values. From these findings, it would seem that patients tested were breathing very nearly at their maximal respiratory ability. If this were true, additional functional demands could be met only if there were a proportionate improvement in respiratory efficiency. In fact, unless such improvement in respiratory function could be achieved, the added functional demands of rehabilitation efforts might well contribute additional acute hypoxia to any chronic hypoxia already present.

Improvement of Respiratory Function

Our efforts to improve efficiency of respiratory function have included use of specific breathing exercises and two mechanical devices. It is usually fairly easy to determine whether there is a relative insufficiency of inspiratory or expiratory efforts, whether atony or spasticity of the abdominal musculature interferes with the normal reciprocal relationship between the abdominal and diaphragmatic musculature, or whether there is a disproportionate movement of the two halves of the thorax. The breathing exercises we recommend[9] are directed toward maximal excursion of the rib cage and improvement in diaphragmatic function. These have been deliberately simplified as much as possible in order that they may be incorporated more easily into the daily activities of the elderly patient.

Intermittent positive-pressure breathing[10] is clinically valuable, especially in treating those patients in whom there is pulmonary emphysema and those who, through chronic illness or prolonged bed rest, have developed atony of the thoracic and abdominal musculature and loss of elastic recoil of the rib cage during expiration. The intermittent positive-pressure device consists basically of a flow-sensitive cycling valve with mouthpiece, gauges, and regulators for the introduction of oxygen in concentrations up to 100% and aerosol solutions containing bronchodilator drugs when these are indicated.

There are many patients who, for a variety of reasons, are unable to eliminate accumulated bronchial secretions satisfactorily.[11] An exsufflator (Cofflator) is effective in meeting this type of pulmonary ventilation need. By means of this device, the lungs are inflated fully with a positive pressure of 30 to 40 mm. Hg followed by a swift reversal to negative pressure of 20 to 40 mm. Hg. This procedure will produce an expiratory volume flow rate several times greater than that produced by a maximal cough and is effective in removing retained bronchial secretions.

Three to five such "coughs" administered once daily, intermittent positive-pressure breathing before and after exercise, and attempts to carry out breathing exercises repeatedly throughout the day have resulted in nearly every case in increased exercise tolerance, less fatigue after exercise, and an improvement in general physical capabilities. An increase of approximately 1,000 cc. in vital capacity has occurred in those patients with the greatest diminution from normal, although all patients increased their vital capacity. Occasionally the increase was so rapid as to cause one to suspect disuse as a cause for diminished respiratory function similar to the diminution noted in other neuromuscular functions. In addition, rather unexpected improvements in patients' attitudes often followed treatment. Patients showed improved outlooks on their physical condition, spontaneous cheerfulness, greater emotional stability, increased attention spans, and increased drives to help themselves.

Early Ambulation

Coupled with efforts to improve respiratory function have been attempts to help the patient achieve ambulation as rapidly as possible. The production of, not necessarily the maintenance of, ambulation activities has been stressed. We believe that the longer the delay in instituting these activities, the greater the difficulty in achieving them. Accordingly, very early use is made of the standing table, so that the proprioceptive-motor patterns of movement can be initiated and exercise of the torso and upper extremity musculature, balance exercises, and breathing exercises can be carried out fairly efficiently with complete lack of fear of falling on the part of the patient. As soon as possible, forward, backward, and side-to-side walking in the parallel bars or with assistance is carried out, with simple, lightweight splinting of a weakened lower extremity when indicated. We have regarded the early achievement of ambulation by the elderly patient as more important than concentrated effort on reeducational exercises for separate areas of weakened muscles.

Summary

Those elderly patients with ailments requiring physical rehabilitation exhibit reduction in efficiency of pulmonary function so frequently that the effects of hypoxia must be included among the etiological factors entering into the disability. Specific retraining efforts for proper breathing coupled with mechanical efforts to increase pulmonary air flow improve the efficiency of external respiration. The increase in exercise tolerance and improvement in certain psychic functions following such treatment would suggest improvement in internal respiration as well. Attempts to stand and to walk at the earliest practicable time, aided by graded exercise procedures, also materially shorten the rehabilitation period.

The assistance of a clinical training fellowship for Dr. Alyea by the Office of Vocational Rehabilitation, Department of Health, Education, and Welfare is acknowledged.

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Coccidioidomycosis.—A correlation between the periodic dust storms occurring in the endemic area and the incidence of new cases of coccidioidomycosis has been noted. These dust storms enable the resistant spores to be transported far from their natural habitat. Cases have been recorded wherein the disease undoubtedly was contracted by the patient merely passing through the endemic area. . . . The majority of those infected with Coccidioides immitis may remain asymptomatic and present no stigmas of active disease. . . . The chest roentgenographic findings, while not specific, often will be the first clue to the diagnosis and will suggest that the physician obtain confirmatory laboratory studies. A rarer, malignant, secondary or disseminated form of this disease occurs approximately once in every 400 cases among the white race, and approximately ten times as frequently in the darker skinned races. This disseminated or granulomatous form of the disease has a mortality of more than 50 per cent.—Capt. W. A. Peck Jr. and Major S. S. Romendick, M.C., U. S. Army, Coccidioidomycosis: A Roentgen Study, *Texas State Journal of Medicine*, February, 1956.

FATALITIES FOLLOWING TOPICAL APPLICATION OF LOCAL ANESTHETICS TO MUCOUS MEMBRANES

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• *The hazards of local anesthesia are due to the rapid absorption of the drug into the vascular system. The etiology of the reactions may be due to a disregard of the amount of anesthetic applied, the use of a topical anesthetic for the first time, or the fact that resuscitative equipment or antidotes were not immediately available. Concerning tetracaine, reactions may be abrupt, with no prodromal signs or convulsions. The dose of tetracaine that may be infiltrated should not exceed 100 mg., therefore the dose for topical application must be considerably less.*

It is surprising that many physicians are unaware of the hazards of local anesthesia. The pioneers in this field recognized and emphasized the pitfalls that result from the misuse of local anesthetic drugs. In 1919, Eggleston and Hatcher[1] studied the toxic effects of procaine, cocaine, and other local anesthetics and indicated that untoward reactions were largely due to the rapid absorption of the drug into the vascular system. Other investigators have since then reiterated this fact. Thus, the potential dangers of these drugs have been known for some time. Those who consistently use local anesthetics are familiar with their hazards. The occasional users are less versed in the subject and usually encounter the majority of difficulties.

Accurate statistics on the frequency of untoward reactions and fatalities due to local anesthetics are not available, because few such mishaps are reported. We are familiar with 10 unreported fatalities in a 15-year period in this institution caused by the topical application of tetracaine to mucous surfaces for endoscopic procedures. In addition, we are aware of five unreported fatalities occurring under similar circumstances outside the institution but in the approximate geographical area. Besides being consulted for the fatalities, we and our associates have been called upon to assist in the treatment and management of numerous other nonfatal reactions. In scanning the protocols of fatalities, one is impressed by the relative frequency with which these have occurred following topical application of local anesthetic drugs. The problem of reactions following the use of local anesthetics, both topically and otherwise, at one time was of such concern, that, in 1924, a commission was delegated by the American Medical Association[2] to review the status of the available drugs and make recommendations concerning dosage and technique of usage. The situation has improved steadily since their report was formulated, but preventable deaths from this cause are still all too frequent.

Characteristics of Tetracaine Reactions

In a review the protocols of fatalities due to tetracaine, the following findings are consistent: 1. The operator had little regard for dosage, was unaware of the maximal allowable quantity, and was unable to indicate the exact amount used. In cases in which the quantity used was known, in most instances it exceeded 8 ml. of a 2% solution (160 mg.). 2. The individual using the drug was a novice learning to do endoscopic procedures. He had used the drug occasionally or was using it for the first time. 3. The reaction was abrupt in onset, without prodromal manifestations. Syncope and circulatory collapse were the usual manifestations. Convulsions did not occur. 4. The drug was used in situations in which resuscitative equipment and antidotes were not immediately available. 5. Barbiturates were used as antagonists in some instances, even though the patient was in respiratory failure and there was no indication for their use.

It is the intent of this report to emphasize the extreme potency and relative frequency of toxic effects from tetracaine and not to incriminate the drug as a lethal substance that should be discarded. Untoward reactions have occurred following the application of other topical anesthetics such as piperocaine, cocaine, and lidocaine. The train of symptoms heralding the untoward response with these, however, has been different. Central nervous system stimulation, characterized by excitement, apprehension, and convulsions, has been the usual manifestation. The intravenous injection of barbiturates counteracted these reactions.

The major distinction between reactions due to tetracaine and those of the other aforementioned drugs has been the absence of convulsions and the abrupt onset of syncope. The interval between the onset of symptoms and the moment of the fatal termination was brief. The train of events occurred so quickly, and in such rapid succession, that there was little time for evaluation of symptoms, differential diagnosis, and antidotal therapy. It must not be construed, however, that convulsions are not manifestations of systemic reactions to tetracaine. They can and do occur with this drug and have occurred in our experience. Convulsions followed the topical application of tetracaine in two instances. These reactions were successfully antagonized by thiopental, and both patients survived.

Cocaine is at the present time the anesthetic of choice for topical use in this institution. Reactions occur from time to time, but none has terminated fatally, even though the total number of reactions and

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Read before the Section on Anesthesiology at the 105th Annual Meeting of the American Medical Association, Chicago, June 12, 1956.

total number of usages far exceed those for tetracaine. Excitement and convulsions have been the usual manifestations of cocaine intoxication.

Postmortem examinations in the aforementioned catastrophes revealed little to suggest the mechanism causing death. For the want of a better explanation, the cause of death was recorded as due to sensitivity to the drug, anaphylactic reaction, allergy, and so on. There was little evidence to substantiate these diagnoses.

The incidence of reactions with use of tetracaine by other routes has been considerably less than with the topical route. Moore,[3] Bonica,[4] and others have described the use of tetracaine for nerve blocking without untoward reactions or fatalities in cases numbering into the thousands. Tetracaine is one of the most widely used drugs for spinal anesthesia. Fatalities due to intoxication following intrathecal injection are unknown. In our experience at the Charity Hospital over a 15-year period, spinal anesthesia has been induced with tetracaine about 20,000 times without a single untoward response suggestive of a toxic reaction. Others have used tetracaine for spinal anesthesia and have had similar experiences. This is probably due to the fact that local anesthetics disappear slowly from the intrathecal space and the over-all dosage is comparatively minute (15 mg. or less). When fatalities have occurred from spinal anesthesia they have been due to severe, uncontrollable hypotension due to the autonomic blockade or from respiratory failure caused by paralysis of the intercostal muscles and the diaphragm due to the ascent of the drug into the thoracic and cervical segments of the cord. Certain clinicians[5] have infused tetracaine slowly, intravenously, without apparent untoward results.

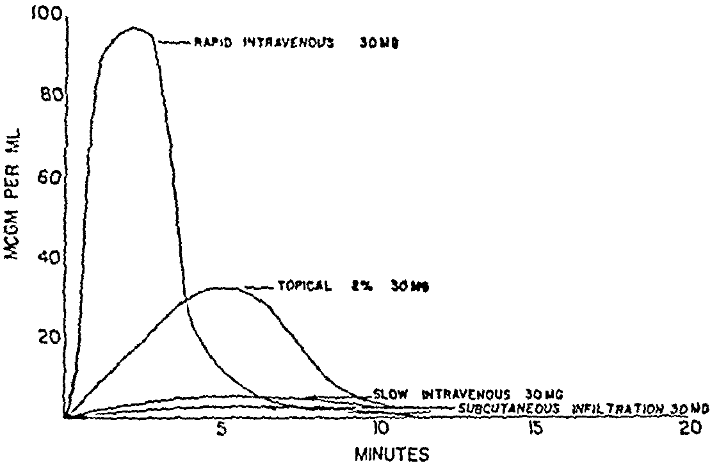

Fig. 1.—Comparison blood levels obtained after injecting 30 mg. of tetracaine in dogs intravenously and rapidly over a 30-to-60-second interval, after application topically to the pharyngeal mucous membranes, after subcutaneous infiltration, and after slow intravenous infusion.

Frequency of Tetracaine Reactions

All of this prompts several questions. "Why are systemic reactions more frequent after topical application?" "Why was sudden syncope the most common manifestation?" It has been suggested that local anesthetics topically applied undergo a change as they pass through the mucous membrane and become "more toxic." We feel this is highly improbable. The symptoms of intoxication following topical application differ in no way from those of reactions due to direct and rapid intravenous infusion of the drug.

Conflicting statements appear in the medical literature concerning absorption of local anesthetic drugs from mucous membranes. Almost everyone assumes that they are rapidly absorbed, but blood level studies to substantiate this assumption are not available. Eggleston and Hatcher[1] indicated the role of rapid absorption in causing reactions but did not determine blood levels. Seevers and his co-workers,[6] studying the metabolism of cocaine, injected the drug subcutaneously, intravenously, and into the stomach but did not study absorption from the pharynx, trachea, bronchi, or other mucous surfaces.

We felt that blood level studies would provide a clue to the cause of high reaction rate and have undertaken this study. For obvious reasons the study was done in the laboratory on dogs. Blood levels were determined after the absorption of tetracaine from mucous surfaces of the pharynx, trachea, and bronchi. These were compared with those obtained after rapid intravenous injection, subcutaneous infiltration, and slow intravenous infusion of tetracaine (fig. 1). The rapid injection of 6 mg. per kilogram of body weight of tetracaine intravenously resulted in peak levels of 100 mcg. or more per milliliter in the circulating blood within one to two minutes. The same quantity applied to the mucous membranes of both pyriform fossae of the pharynx or instilled into the trachea resulted in peak levels of 30 mcg. per milliliter. The peak was attained within four to six minutes. The peak was not as high, nor did it rise as abruptly, as that noted after rapid intravenous injection, but it obviously simulated it closely. There was little difference between the curves obtained after the pharyngeal and tracheal instillations. Epinephrine, 1:7,500, added to the tetracaine solution did not retard absorption. The blood levels were nearly identical to those obtained without epinephrine.

In one set of experiments the total dose was doubled, divided into three fractions, and applied at equal intervals over an 8-to-10-minute period. The blood level gradually attained a peak of 20 mcg. per milliliter after 10 minutes. Thus, it is obvious that the gradual application of a solution results, as one would expect, in a gradual rise in blood level. It is important to note that identical blood levels were obtained when the total dosage in milligrams remained constant but the concentration was varied from 2 to 4%. Thus, the blood level is a function of total dosage and not of concentration (fig. 2). The blood level was not detectable when 6 mg. per kilogram was infiltrated subcutaneously in an area 3 by 4 cm. over the abdomen. The slow intravenous infusion of 6 mg. per kilogram over a 20-minute period likewise caused no detectable quantity in the blood after the injection was complete.

The free base was precipitated and applied to the mucous membranes. The blood level curves were identical to those obtained when solutions of the hydrochloride were used. The absorption of the hydrochloride incorporated in a water-soluble cream applied to mucous surfaces is prompt and rapid and occurs with ease. These data indicate what has not been realized, namely, that the topical application of a given dose results in blood levels that closely simulate those obtained after rapid intravenous injection.

The epithelial surfaces of the pharynx, trachea, and the posterior urethra provide excellent absorbing surfaces. Drugs are readily absorbed from the pulmonary alveoli because the osmotic pressure relationships in the pulmonary vascular bed are designed to prevent collection of fluid in the alveolar spaces. Volunteers inhaling free nebulized cocaine (4%) immediately experienced the stimulation characteristic of this drug and felt no appreciable numbness in the upper respiratory passages.

Circulatory Effects

Most physicians are generally aware of the effects of these drugs on the central nervous system; they are less familiar with the circulatory effects. Local anesthetics depress cardiac tissues.[7] The myocardium may be so depressed that asystole results. This depressant effect of local anesthetics has been utilized to prophylactically decrease cardiac irritability and thus obviate arrhythmias during thoracic surgery. Eggleston and Hatcher[1] demonstrated that digitalis administered prior to the infusion of toxic doses of local anesthetics protects animals from cardiac failure. Local anesthetics also cause vasodilatation. Extreme hypotension occurs when myocardial depression and vasodilatation occur simultaneously. There is no reason to assume that both the circulatory and nervous systems cannot be involved simultaneously, particularly when overwhelming doses are used. In fact, the evidence in some of the protocols suggests that this is exactly what happens. Circulatory and respiratory failure occurred simultaneously. The circulatory effects of tetracaine are exemplified by the following case report.

Report of a Case

A 67-year-old white woman was admitted to the hospital for diagnostic bronchoscopy for a possible carcinoma of the lung. She was given premedication of morphine, 1/6 grain (10 mg.), and scopolamine, 1/100 grain (0.6 mg.), one hour prior to the time of her arrival in the operating room. The nasopharynx was sprayed with a 2% solution of tetracaine. An estimated 5 ml. was then instilled into the trachea with a curved cannula. The operator made no note of the total dose used. Several minutes after application of the anesthetic, the patient uttered a sharp cry and slumped over from the upright position. An ashen gray cyanosis appeared over her face and neck. She became comatose. She was placed in a supine position. The pulse was thready and barely palpable. The blood pressure was unobtainable. The neck veins were engorged. Respiration was shallow and rapid. Administration of ephedrine, 15 mg., caused a feeble fleeting pressor response, after which the blood pressure disappeared. Additional doses were ineffective. Pulmonary edema then developed. Oxygen under positive pressure was administered by mask. Attempted digitalization with ouabain was futile, and death ensued one and a half hours after injection of the drug. There was no evidence of preexisting cardiac disease. The train of symptoms developed within three to four minutes after the instillation of the drug. The bronchoscopy had not commenced; hence, the cause of death was ascribed to cardiac failure.

Of the drugs possessing topical action, dibucaine and tetracaine are the most potent and most toxic. Procaine, the least toxic local anesthetic in current use, is devoid of topical action. Most endoscopists concede that tetracaine is the most serviceable drug from the standpoint of effective topical anesthesia. The term "potency" applied to topical anesthetics is not easily defined. Tetracaine, for example, when directly applied to a nerve trunk, is 10 times more potent than procaine. In other words, 1 mg. causes a blockade when 10 of procaine are necessary to obtain the same effect. However, potency is difficult to dissociate from duration of action. Tetracaine, in addition to being more potent on a weight-for-weight basis, causes a blockade that lasts approximately twice as long as that of procaine. With the exception of dibucaine, which few clinicians use, it is the longest lasting of the available topical anesthetics.

Evaluation of Topical Action

The topical effects of local anesthetics are not easily evaluated. In the laboratory, topical action is usually studied by applying a fixed quantity of a drug to the cornea of experimental animals and noting the duration of absence of the corneal reflex. Such studies merely suggest trends as far as the value of a drug for clinical use is concerned. In clinical evaluation of these drugs, the variables encountered are too numerous to make a study clear-cut and simple. The types, sizes, and arrangement of cells composing the mucous surfaces, the blood supply, the nature of the submucous tissue, and the type of neuroreceptors present introduce a multitude of variables. Some of the pain felt during instrumentation of mucous surfaces undoubtedly arises in the submucous areas where the drugs do not necessarily penetrate in sufficient concentration to cause effective blockade. A possible answer to the existing impression that tetracaine appears to be superior to other topical anesthetics may be that it anesthetizes these deeper structures more effectively and for a longer period of time.

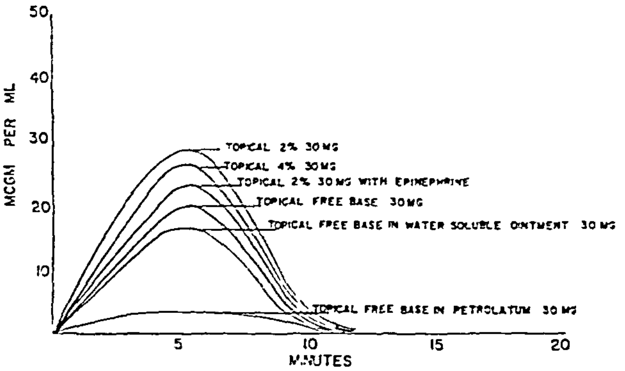

Fig. 2.—Comparison of blood levels of tetracaine in dogs after application to the mucous membranes of tetracaine hydrochloride. 30 mg. of the free base, 30 mg. in 2 and 4% solution with and without epinephrine, 30 mg. in a water soluble base, and 30 mg. in a non-water-miscible base.

In our studies conducted in 23 volunteers, it was observed that the order of duration and degree of numbness experienced for topical anesthestics applied to the mucous surfaces of the palate, lip, site of the tongue, and the fauces is as follows: tetracaine, cocaine, lidocaine, piperocaine, hexylcaine, benzocaine, tripelennamine (Pyribenzamine), and pramoxine (Tronothane). A latent period precedes the onset of local anesthesia whether the agent is topically applied or injected. The longest period preceded tetracaine; the shortest, benzocaine. Since the degree of numbness was used to indicate potency of the topical effect of the drug and since this is a subjective manifestation, one is justified in challenging these results. We, however, know of no other effective way of studying the clinical usefulness of these substances.

Water solubility of a drug and its ability to diffuse through membranes play important roles in topical anesthesia. Benzocaine, for example, is poorly soluble in water (0.5 gm. per liter). When applied to a mucous surface, it is absorbed more slowly than cocaine, tetracaine, and other drugs. Untoward reactions due to systemic toxic effects are virtually unknown from use of this substance. An ointment containing 20% benzocaine (Americaine) has been used in this department nearly 10,000 times as a lubricant for intratracheal catheters and for pharyngeal and nasal airways to obtund the pharyngeal and tracheal reflexes without any untoward effects.

Dosages

It is impossible to state the lethal doses of the different anesthetics for man because such doses vary with the route of administration, rate of absorption and elimination, and tolerance of the individual to the drugs. Values are often quoted that are based upon lethal doses in animals or on impressions derived from clinical experience. Such data merely indicate trends and are useful as guides but are not absolute values.

Thus, it cannot be emphasized too strongly that when a drug is applied topically a maximum total dosage must be decided upon that must not be exceeded at any one sitting. Tetracaine is considered to be 10 times more toxic than procaine. On the basis that 1 gm. of procaine is the maximum quantity recommended for infiltration, it follows that 100 mg. of tetracaine must not be exceeded for infiltration. Furthermore, when topical application is used, allowance must be made for the greater ease of absorption from the mucous membranes. The total quantity, therefore, should be considerably less than that used for infiltration. Carabelli[8] has obtained adequate anesthesia with a 0.25% solution of tetracaine. He suggests a maximum limit of 20 mg. applied in fractional doses. Rubin and Kully[9] suggest 50 mg. as the upper limit. This must be applied in fractions over a period of 15 to 20 minutes. Wiesel and Tella,[10] using quantities not exceeding 40 mg. for 1,000 endoscopic procedures, noted 19 reactions. Seven of these were convulsive. The remainder were classified as "mild circulatory." There were no fatalities. It is obvious, then, that quantities of 180 to 200 mg., which were associated with death, were excessive.

Treatment of Reactions

In the event a serious reaction occurs, one is faced with the problem of respiratory failure and asystole. If cardiac arrest is suspected, immediate opening of the thorax and cardiac massage is indicated. If the heart has not stopped but the blood pressure is unobtainable, vasopressors such as ephedrine, methamphetamine (Desoxyephedrine), or methoxamine or other similar drugs should be administered intravenously. Artificial respiration must be instituted immediately and maintained throughout the period of apnea. Obviously one should not undertake the topical administration of local anesthetics where it is not possible to immediately institute resuscitative measures.

Summary and Conclusions

Fatalities and untoward reactions occur more frequently when local anesthetics are used topically than when they are administered by other routes. Rapid absorption has been presumed as the cause, but data in support of this contention have not been available. Studies of blood levels of tetracaine indicate that this occurs and at a more rapid rate than has been supposed. A quantity of drug that results in no detectable blood level when infiltrated subcutaneously gives levels when applied topically that are equal to one-third to one-half of those after intravenous injection. The untoward responses are due to the rapid passage of the drug from the site of application into the systemic circulation. The absorption from mucous membrane is far more rapid than clinicians have realized and simulates intravenous administration. Study of the fatalities that have occurred indicates that the cause of death is overdosage from rapid absorption.

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Shock.—The clinical syndrome of shock is well known to all physicians, but for purposes of this discussion, shock is considered to be present when, in a previously normotensive patient, the systolic pressure is 80 mm. Hg or below, accompanied by the signs of circulatory collapse such as cyanosis; cold, clammy, moist skin; rapid, thready pulse; and narrowed pulse pressure. In patients with pre-existing hypertension, the clinical syndrome of shock may be present when the systolic pressure is 100 mm. Hg or even higher, depending on the degree of hypertension existing previously.—F. N. Talmers, M.D., T. J. Regan, M.D., and H. K. Hellems, M.D., Review of Pathophysiology and Treatment of Shock Accompanying Myocardial Infarction, *Journal of the Michigan State Medical Society*, March, 1956.

EVALUATION OF CORTISONE IN THE TREATMENT OF CEREBRAL INFARCTION

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• *Thirty-six patients brought to a hospital with symptoms of cerebral infarction were classified as to the severity of the condition and divided into two groups comparable as to severity, age, blood pressure, and other essential criteria. Both groups received the usual supportive care. The test group of 17 patients received, in addition, 300 mg. of cortisone and 3 gm. of potassium chloride daily with a low-salt diet. The cortisone was given in divided doses, and the dosage was reduced after the second day. The contra-test group of 19 patients received a placebo. There were 13 deaths in the cortisone and 10 in the placebo group. The difference, though small enough to have arisen by chance, discouraged further use of cortisone in this situation. The classification according to severity was found to have prognostic value, and an impressive number of patients were seen who could not be admitted to either group because their symptoms cleared up spontaneously within a few hours. Cortisone must not be used indiscriminately. Its unfavorable effects in this series of patients occurred despite observance of known contraindications. Emphasis in cases of cerebral infarction should be on general supportive treatment.*

The high incidence of cerebral vascular disease in the United States confronts physicians with a vital problem. In addition to being the third highest cause of death in this country, cerebral vascular disease is attended by a high degree of morbidity. In 1952, it was estimated that 170,000 persons died from this type of disease. At that same time it was estimated that there were 1,800,000 survivors from previous years, each with residuals of varying degree. Of those who died, 44,000 were in the productive age group 25-65.[1] The scope of this problem indicates the need for intensified, adequate research pertaining to the causes and treatment of this type of disease.

In spite of much research, no truly effective means of treating cerebral vascular disease has yet been discovered. Many of the articles refer to supportive care as being the only treatment available; certainly in cerebral hemorrhage the mortality figures attest to the inadequacy of this form of treatment.[2] With cerebral infarction, however, there is more hope and there are interesting theoretical possibilities for treatment. Cerebral infarction can occur secondary to an embolus or thrombus, but in over 60% of the brains showing infarction no embolus or thrombus could be found.[1] This observation has given rise to several stimulating theories as to the cause of the infarctions. Among the proposed causes has been arterial spasm,[3] producing changes in blood flow and blood pressure, relative ischemia, and tissue destruction.[4] Even in infarction due to emboli or thrombi, dissolution and fragmentation of the emboli and thrombi could occur as part of the general process.

Regardless of the mechanism at the onset, it is probable that there first occurs an area of necrosis in the area completely dependent on the occluded vessel and, surrounding this, an area of tissue reaction characterized by ischemia and edema. This secondary area gradually becomes necrotic, with development of further tissue reaction; in this manner the infarction may theoretically propagate itself. If the blood flow to this ischemic area could be increased or the surrounding tissue reaction decreased, ultimate recovery of the area might be possible. There would be more prompt recovery and fewer residuals. In addition, the mortality would be lowered by shortening the critical phase associated with the secondary infections that frequently follow bed rest in older patients.

Attempts at therapy have been multiple. Use of bilateral stellate ganglion blocks has been both widely supported and condemned.[5] Its value has not been supported by results in an adequately controlled series of cases. Several agents, such as papaverine, carbon dioxide, and procaine hydrochloride,[6] raised false hopes, which were shattered when their use was evaluated in larger controlled series. At the present time, preventive therapy with anticoagulants appears to be of some value in specific types of cerebral vascular disease; at least the anticoagulant drugs promise to prevent the development of new symptoms and signs.[7]

In a recent report, cortisone was described as remarkably decreasing morbidity, mortality, and the estimated ultimate deficit in acute cerebral infarction.[8] Because of the potential dangers and complications associated with the use of cortisone, it was thought desirable to attempt a further evaluation of this drug under controlled conditions.

Method of Study

In general, the method used was to admit all patients to the neurological service as soon as possible after the onset of symptoms. At that time they were placed in groups according to the severity of the disease, the degree of severity being determined by various factors (table 1). The index to severity was established by previous personal observations and other observations in the literature.[5f] After being assigned to severity groups, the patients were alternately treated within each severity group either with cortisone or with placebo. In addition, at all times during this series one of us (P. T. W.) checked on the evaluation of the severity of the patient's condition and on the ultimate progress of the case, without having knowledge at any time as to the drug the patient was receiving. The steps followed in evaluation and treatment are discussed in more detail below.

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9. Footnotes 3*a* and 4.

CLINICAL NOTES

SEVERE CITRATE INTOXICATION DURING CARDIOVASCULAR SURGERY

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Over the past years a number of authors have called attention to the potential dangers of a decrease in the ionized calcium level in blood of recipients of large volumes of citrated blood. Citrate intoxication has become a common problem during replacement of a large volume of blood in exchange transfusions, in the more aggressive management of various types of hemorrhage, and during cardiovascular surgery. A progressive fall of the ionized calcium level in the blood may cause tetany, prolongation of the Q-T interval and S-T segment of the electrocardiogram, prolongation of mechanical ventricular systole, hypotension unresponsive to further infusions of citrated blood, and finally cardiac arrest. Citrate intoxication may rarely be responsible for some impairment of the coagulation mechanism.[1]

The clinical warning signs of muscle tremors and tetany are usually absent in patients in deep shock or in surgical anesthesia, and, since there is no readily available laboratory procedure for the determination of the ionized calcium level of blood, the electrocardiogram usually provides the most useful indication of the development of citrate intoxication. In the case reported, rather extreme electrocardiographic and hemodynamic changes developed due to citrate intoxication in a patient with the tetralogy of Fallot undergoing an infundibular resection. Since during such procedures we routinely monitor the electrocardiogram and record right ventricular and pulmonary artery pressures, a fortuitous delay in obtaining calcium for administration allowed observations on these and other physiological variables during development and restitution of advanced citrate intoxication.

Report of a Case

A 24-year-old woman had been moderately cyanotic since birth. In recent years there had been progression of cyanosis and increasing dyspnea on exertion. Cardiac catheterization and other studies confirmed the clinical diagnosis of tetralogy of Fallot. The resting arterial oxygen saturation was 62% and the hemoglobin level equal to 22 gm. per 100 cc.

On April 3, 1956, an infundibular resection was carried out through a purse-string incision in the anterior portion of the right ventricle. At the start of the procedure the systemic blood pressure was 98/65 mm. Hg; the right ventricular pressure, 110/5 mm. Hg; the duration of right ventricular systole, 0.36 sec.; and the corrected Q-T interval of the electrocardiogram ($Q\text{-}T_c = Q\text{-}T/\sqrt{R\text{-}R}$), 0.46 sec. (see figure, *A*). Blood was infused under pressure according to the estimated amount of blood lost at cardiotomy, and over the course of the first 15 minutes of the infundibular resection the blood losses amounted to about 500 cc. (see figure, *B*). Over the next few minutes an additional 250 cc. of blood was administered and definite prolongation of $Q\text{-}T_c$ became apparent but was disregarded because of the small amount of blood that had been transfused to that point (see figure, *C*). With continued administration of blood, definite evidence of citrate intoxication became apparent with further prolongation of $Q\text{-}T_c$, a fall in right ventricular systolic pressure, and a drop in systemic arterial pressure to 50 mm. Hg systolic. Technical delay in administering the calcium allowed further observations of electrocardiographic changes as the infusion of blood was continued. Notwithstanding an increased rate of infusion of blood, the systemic arterial pressure became unobtainable and there was further prolongation of $Q\text{-}T_c$, with development of broadening and change in the contour of QRS and depression of the S-T segment (see figure, *E* and *F*). The duration of right ventricular systole was increased from 0.36 sec. at the start of the procedure to 0.49 sec. just prior to the administration of calcium. There was a period of cardiac arrest lasting for four or five cycles, with resumption of contractions after three or four cycles of massage. At this point, 4 cc. of a 10% solution of calcium chloride was injected directly into the cavity of the right ventricle; within three minutes the systemic pressure had risen to 80/60 mm. Hg and $Q\text{-}T_c$ had shortened from 0.71 sec. to 0.54 sec. (see figure, *G*). An additional 5 cc. of 10% calcium chloride solution was given intravenously, and within 10 minutes the systemic blood pressure had risen to 110/85 mm. Hg and the electrocardiogram had returned essentially to the configuration obtained at the initia-

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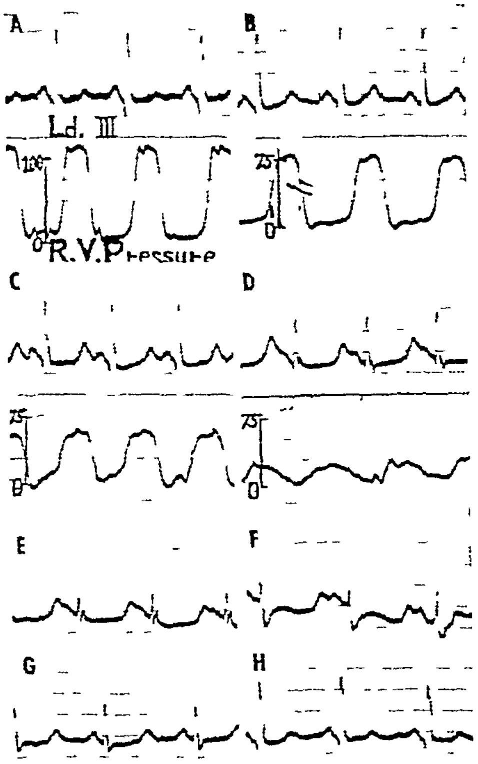
tion of the procedure (see figure, *H*). Approximately 1,500 cc. of citrated blood was administered from the start of the procedure until the time the calcium chloride was administered; the last 1,000 cc. was infused over approximately 15 minutes (each unit of blood consisting of 440 cc. of donor blood and 110 cc. of anticoagulant acid-citrate-dextrose solution B). The patient's postoperative course was uncomplicated.



Electrocardiographic studies of 24-year-old woman *A*, lead 3 of electrocardiogram and right ventricular pressure wave at start of infundibular resection Q-T_c = 0.46 sec, systemic arterial pressure = 98/65 mm Hg, right ventricular pressure = 110/5 mm Hg, and duration of right ventricular systole = 0 36 sec. *B*, 15 minutes after start of resection, 500 cc. *of* citrated blood had been administered Q-T_c = 0.5 sec., systemic pressure = 90/60 mm. Hg, right ventricular pressure = 80/5 mm Hg, and duration of right ventricular systole = 0 42 sec *C*, *after an additional* 250 cc. of citrated blood, Q-T_c = 0 6 sec., systemic pressure = 85/60 mm. Hg, right ventricular pressure = 60/5 mm. Hg, and duration of right ventricular systole = 0 42 sec *D*, after an additional 350 cc *of citrated blood,* Q-T_c = 0.66 sec., systemic systolic pressure = 50 mm Hg, right ventricular pressure = 20/0 mm Hg, and the duration of right ventricular systole = 0.49 sec *E*, after an additional 200 cc. of citrated blood, Q-T_c = 0.67 sec., there is notching of QRS and depression of the S-T segment The systemic blood pressure was unobtainable. *F*, after another 200 cc. of citrated blood, Q-T_c = 0.71 sec, a broad S wave has developed, QRS has been prolonged to 0.1 sec, and there is further depression of S-T. *G*, 3 minutes after intracardiac injection of 400 mg. of calcium chloride, Q-T_c = 0 54 sec *H*, 15 minutes after intravenous injection of an additional 500 mg of calcium chloride intravenously, Q-T_c = 0.47 sec and electrocardiogram shows little difference from *A*.

Comment

Recent clinical and laboratory studies have indicated renewed interest in the problem of citrate intoxication and awareness of its increasing incidence. Bunker and associates [1] have recently presented clinical studies of several aspects of citrate intoxication. Furman and associates [2] and Gustafson [3] have presented studies of the electrocardiogram during exchange transfusions in erythroblastotic infants. Cookson and associates [4] have indicated the hazards of citrated blood during cardiac surgery and hypothermia. In the case herein reported approximately one-third of the patient's blood volume was replaced by citrated blood in a period of about 30 minutes. The electrocardiographic changes in this case were more marked than have usually been reported. They included a progressive increase in Q-T_c from 0.46 sec to 0.71 sec. There was depression of the S-T segment, with some increase in the amplitude of the T waves. At the height of the changes there was delay in interventricular conduction with change in the form of the QRS complexes. There was a progressive fall in the systemic arterial pressure and the systolic pressure in the right ventricle that was unresponsive to further infusion of citrated blood. Just prior to the calcium injection the heart began to dilate, the rate slowed, and there was sinus arrest for several cycles. With dilatation of the heart, there was further drop in the systolic pressure in the right ventricle and prolongation of mechanical systole. but, in spite of the feeble contractions, the end diastolic pressure in the right ventricle did not rise. All these changes were completely reversed within a few minutes after the injection of rather small amounts of calcium chloride.

Summary

Rather extreme cardiovascular changes occurred due to citrate intoxication in a young woman with the tetralogy of Fallot undergoing an infundibular resection. All changes were promptly reversed by the administration of small amounts of calcium chloride.

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Atherosclerosis.—The lipoproteins in the bloodstream constitute an entire spectrum of molecules, varying in size and density from the giant chylomicra—in which form alimentary neutral fat is carried in the thoracic duct—down to the smallest high-density particles. Gofman and his coworkers believe that the sequence of lipoprotein molecules represents a chain in which *metabolic* interconversions are going on in the blood. The largest particles are composed predominantly of neutral fat, and this component diminishes with decrease in particle size. Following the injection of heparin, lipemia clearing can be demonstrated and ultracentrifugal analysis reveals a decrease in the larger low-*density lipoproteins*. The total amount of circulating fat is reduced. Since heparin is normally present in the bloodstream, and the lipemia clearing process has been demonstrated in human plasma without prior injection of heparin, this mechanism is probably physiologic. It is involved in the transport and disposal of absorbed alimentary neutral fat. Failure or deficiency of the process might well be of fundamental significance in the accumulation of excessive quantities of low-*density* or beta lipoproteins in the circulating blood. Thus a heparin deficiency has been suggested by various workers as a possible etiologic factor in serum lipid metabolic defects.—H. Engelberg, M.D., The Prophylactic Management of Coronary Atherosclerosis, *Geriatrics*, June, 1956.

J.A.M.A., December 22, 1956

COUNCIL ON PHARMACY AND CHEMISTRY

Report to the Council

The Council has authorized publication of the following report. Nonproprietary terminology is used for drugs that are mentioned; when such terminology is not considered to be generally well known, its initial appearance is supplemented by parenthetic insertion of names known to be applied to commercial preparations. H. D. KAUTZ, M.D., *Secretary.*

CURRENT STATUS OF THERAPY IN SYPHILIS

Evan W. Thomas, M.D., Albany, N. Y.

The therapeutic agent of choice for all types of syphilis is penicillin, unless a patient is sensitive to penicillin, in which case other antibiotics may be used. The Treponema pallidum is extraordinarily sensitive to penicillin. No proved penicillin-resistant strains of the organism have been found. As a rule, relatively low blood concentrations of penicillin, sustained for 7 to 10 days in early and latent syphilis and for 10 to 20 days in late symptomatic cases, are sufficient to cure or permanently arrest the infection. Rarely, a patient may require more intensive treatment with preparations that provide higher blood concentrations of penicillin sustained over a longer period than is needed for the great majority of patients. Reasons for this are obscure, but it is possible that in rare cases penicillin is absorbed poorly from muscle depots. Whether or not this is true, increasing the total dosage of penicillin for the treatment of syphilis in relatively large series of patients beyond the amount found to be effective in the great majority of cases has not significantly lowered the number of patients who had to be re-treated. Consequently, in the routine treatment of syphilis, there seems to be little reason to exceed total dosages of penicillin that have proved to be adequate in 85 to 95% of cases.

The treatment schedules advised in this article are minimal. They are based on experience with relatively large series of cases that have been followed up for at least two or more years after therapy. It must be recognized, however, that by far the largest series of patients with such a follow-up were treated with penicillin preparations that preceded benzathine penicillin G (Bicillin; Permapen). The advantages of this new preparation are so great that it cannot be omitted from any discussion of modern antisyphilitic therapy. Despite the relatively meager data on prolonged follow-up of patients treated with this very slowly absorbed preparation, it promises to supersede other types of penicillin in the treatment of syphilis. A single treatment with 2,400,000 units of benzathine penicillin G provides demonstrable blood concentrations of penicillin for at least 15 days. Because of the slow absorption, blood levels of penicillin are low but sufficiently high for the treatment of most cases of syphilis, with the possible exception of relapses and infections of the cardiovascular and central nervous systems.

Classification of Syphilis

In outlining the treatment of syphilis, the disease can be classified into three main divisions: (1) early symptomatic syphilis, which includes the primary and secondary stages; (2) latent or asymptomatic syphilis diagnosed solely by serologic tests and history; and (3) late symptomatic syphilis.

Latent syphilis has long been classified as early or late. Early latent syphilis is defined by some authorities as an infection of less than 2 years' duration and by others as one of less than 4 years' duration. Which definition is chosen depends upon how long one believes the immunologic status of early syphilis lasts. Actually the duration of this status probably differs greatly in different individuals, and, for the purpose of treatment, there is no reason to believe that either early or late latent syphilis requires more or different therapy than does secondary syphilis. However, in evaluating the results of therapy, it has been found that early latent syphilis of less than one year's duration usually becomes seronegative after treatment much more rapidly than does latent syphilis of longer duration.

Treatment Schedules for Primary and *Secondary Syphilis*

A single treatment with 2,400,000 units of benzathine penicillin G is advised for routine treatment of early symptomatic syphilis. This dosage is best given by an injection of 1,200,000 units (4 cc.) in each buttock. A single injection of 4 cc. of a preparation containing 600,000 units per cubic centimeter can be given, but this concentrated suspension has caused incapacitating pain at the site of injection in some individuals. Smith and Shafer and co-workers of the U. S. Public Health Service have reported as good results with a single treatment of 2,400,000 units of benzathine penicillin G as with 4,800,000 units or more of procaine penicillin G in oil and aluminum monostearate given in divided doses over 7 to 21 days. Their findings are based on the follow-up of a series of 196 cases.

If procaine penicillin G in oil and aluminum monostearate is used, the advised dosage is 4,800,000 units given in divided doses of 1,200,000 units at intervals of 2 to 7 days. No advantage has been found in giving individual doses smaller than 1,200,000 units, and some

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Venereal Disease Consultant, New York State Department of Health.

data suggest that better results have been obtained when injections were given at intervals of 2 to 4 days than at longer intervals.

Evaluation of Treatment of Primary and Secondary Syphilis

Quantitative serologic tests for syphilis are of great help in the follow-up of patients treated for early symptomatic syphilis. Seronegative primary cases may become seropositive immediately after therapy, but the tests should again be negative within a month after successful therapy. Cases of primary or secondary syphilis seropositive at the time of treatment should show definite drops in titers within 6 months after successful therapy. Complete seronegativity may not be obtained for a year or more, but as long as the drop in titers to low levels is maintained, re-treatment is unnecessary. Available data on large series of patients indicate that 20% or more with secondary syphilis remain seropositive in low titers (positive in dilutions of 1 to 2 or less) for 1 to 5 years after successful treatment.

Re-treatment is indicated when a rise of titers from previous levels occurs or when clinical relapse is evidenced by lesions of the skin or mucous membranes. In the absence of clinical relapse, a single rise in titers from previous levels should always be confirmed by repeated tests. When serologic titers are determined at weekly or monthly intervals, it is not unusual to find that increases in the titer of a single test are not sustained at subsequent tests. Relapse or reinfection is associated with rapid and marked increases in titers.

As a rule, a reinfection requires no more treatment than an original infection, but a relapse should be treated more intensively with procaine penicillin G in oil and aluminum monostearate rather than with benzathine penicillin G because of the higher concentrations of penicillin obtained with the former preparation.

Treatment Schedules for Latent Syphilis

When diagnosis of latent syphilis is made, asymptomatic neurosyphilis should be ruled out by spinal fluid examination and cardiovascular syphilis by fluoroscopic examination or teleroentgenography. No good evidence exists that latent syphilis, early or late, requires more treatment than does secondary syphilis; therefore, the treatment schedules advised for secondary syphilis may be used for latent cases.

When the diagnosis is doubtful, because of failure to obtain a spinal fluid examination or to rule out cardiovascular involvement, a single treatment with 2,400,000 units of benzathine penicillin G would probably be effective for most patients with asymptomatic neurosyphilis; however, available data are insufficient to decide this question one way or the other. When in doubt, a total dosage of 6 million units of procaine penicillin G in oil and aluminum monostearate given in doses of 1,200,000 units at intervals of 2 to 7 days should provide sufficient therapy for patients with asymptomatic involvement of the central nervous or cardiovascular systems.

Evaluation of Treatment of Latent Syphilis

A noticeable and relatively rapid decline in serologic titers during the first 6 months after successful treatment can be expected when early latent syphilis has been present for less than one year. When the infection has been present for more than one year, prolonged persistence of seropositivity is the rule. Relatively high titers usually decline within one year after treatment, but occasionally it is impossible to obtain low titers by any regimen of treatment. Persistence of positive serologic tests for syphilis for years after treatment of late latent or late symptomatic syphilis does not necessarily mean a continuation of the infection. Treatment for the sole purpose of obtaining negative titers is usually futile.

Indications for re-treatment are the development of symptoms attributed to syphilis or of sustained increases in serologic titers from previous levels. Development of the latter must be determined with caution. Titers are determined by diluting the serum. They are usually reported as positive in undiluted serum or in dilutions of 1:2, 1:4, 1:8, 1:16, and so forth. The practice of doubling the dilution at each successive step may be disconcerting to the physician unless this is understood. A reported titer of positive in dilutions of 1:16 might be positive in dilutions of 1:32 in a subsequent test without the increase being significant; a later test might again be reported as positive in dilutions of 1:16. To be significant, an increase in reported titers should be more than one step in the dilutions and the increase should be sustained for several months before re-treatment is given. In a prolonged follow-up of treated patients, it is not unusual for reported titers to fluctuate at times between lower and higher levels.

Treatment of Late Symptomatic Syphilis

No data are as yet available on the follow-up of significantly large series of patients treated for late symptomatic syphilis with benzathine penicillin G. If this preparation is used, it seems advisable to give at least three treatments of 2,400,000 units at intervals of no more than 7 days. The purpose of this treatment is to increase the concentration of penicillin within the body rather than to prolong the duration of treatment.

Good results have been obtained in the treatment of neurosyphilis with procaine penicillin G in oil and aluminum monostearate. Serial spinal fluid examinations afford means, which are unavailable in cardiovascular syphilis, of evaluating treatment of this complication. On the basis of spinal fluid examinations, total dosages of 6 to 10 million units of this form of penicillin are sufficient for over 90% of all types of neurosyphilis, including paralytic dementia and primary optic atrophy. This does not mean that symptoms caused by irreversible changes in nervous structures can be relieved or that far-advanced cases of primary optic atrophy may not progress to blindness. The time to treat syphilis is before such advanced pathological changes have occurred.

By analogy with neurosyphilis, treatment with 6 to 10 million units of procaine penicillin G in oil and aluminum monostearate can be advised for all types of late symptomatic syphilis. Individual doses, consisting of 1,200,000 units, may be given two or three times a week.

Evaluation of Treatment of Late Symptomatic Syphilis

As is true of late latent syphilis, treatment of late symptomatic syphilis is not followed in most patients by seronegativity within 10 or more years. Regardless of the kind, amount, and duration of therapy, 70% or more of large series of patients treated for late latent and late symptomatic syphilis have been seropositive 10 years after treatment.

Re-treatment is advised when titers increase significantly from previous levels and the increase is sustained for several months. Even in the absence of increased serologic titers, progression or relapse of symptoms and signs attributed to syphilis may be an indication for additional therapy, but it is by no means true that active syphilis is always the cause of such presumed progression. Causes other than syphilis may adversely affect tissues already severely injured by syphilis that has been inactivated by treatment.

The best guide to the activity of neurosyphilis is serial spinal fluid examinations performed at 6-month intervals. Pleocytosis (lymphocytes and other mononuclear cells in the spinal fluid) in association with positive specific tests for syphilis in the spinal fluid indicate disease activity. After treatment, cell counts should be less than 4 per cubic millimeter within 6 months to a year; high total protein content of the spinal fluid at the time of treatment should decline within a similar time, but the total protein determinations may not be within normal limits for a year or more. High titers of specific tests for syphilis in the spinal fluid at the time of treatment should show a decline within one year after treatment, but the tests generally do not become negative for years. Relapse of neurosyphilis is indicated by the reappearance of increased cell counts and frequently by increases in the total protein and in quantitative specific tests for syphilis in the spinal fluid. Titers of the blood serologic tests may or may not increase in the presence of relapsing neurosyphilis.

Unfortunately, a word of caution regarding the reports of cell counts, total protein values, and colloidal gold tests of spinal fluid is necessary. Unless these tests are made with reasonable accuracy and consistency, the reports may be more confusing than helpful. In the absence of complete and reliable spinal fluid examinations for neurosyphilis, patients might well be spared the ordeal of repeated spinal punctures. On the basis of experience at Bellevue Hospital in New York City where spinal fluid examinations were made by specially trained personnel, 6 to 9 million units of penicillin, acting over 15 to 20 days, should inactivate neurosyphilis in over 90% of patients.

Treatment of Syphilis in Pregnancy

Syphilis in pregnant women requires no more or different therapy than in nonpregnant women. The question always arises as to whether the woman who has acquired syphilis should be treated in each succeeding pregnancy. In general, available data indicate that this is unnecessary, provided the woman has received previous penicillin therapy with no subsequent evidence of relapse or reinfection. When there is doubt about the adequacy of previous treatment, a single treatment with 2,400,000 units of benzathine penicillin G or four injections of 1,200,000 units of procaine penicillin G in oil and aluminum monostearate should be given during pregnancy. When syphilis is discovered very late in pregnancy, it is always advisable to treat it as soon as possible. Even when treatment is given only a few days before delivery, the fetus may benefit by the therapy as penicillin crosses the placenta to the fetus.

Treatment of Congenital Syphilis

Congenital syphilis can be treated in the same way as acquired syphilis except that smaller doses should be used in children weighing under 32 kg. (70 lb.). Infants and children should receive total doses of 75,000 to 100,000 units of penicillin per kilogram of weight. Procaine penicillin G in oil and aluminum monostearate in doses of 0.5 to 1 cc. (150,000 to 300,000 units) may be injected every 2 to 4 days until the total dosage is completed.

Substitutes for Penicillin

Antibiotics other than penicillin may be used to treat syphilis in patients sensitive to penicillin. Oxytetracycline hydrochloride (Terramycin Hydrochloride), chlortetracycline hydrochloride (Aureomycin Hydrochloride), chloramphenicol (Chloromycetin), erythromycin (Erythromycin; Ilotycin), erythromycin stearate (Erythrocin Stearate), and carbomycin (Magnamycin) are effective antisyphilitic agents. Data on their use are limited, the greatest experience having been with the first two. Turner and Schaeffer have recently reported that, in the laboratory, T. pallidum is more sensitive to erythromycin and carbomycin than to any of the other antibiotics except penicillin.

It is doubtful that minimal effective dosages of the antibiotics other than penicillin have been determined. From the available data, it appears that early and latent syphilis should be treated orally with at least 3 to 4 gm. daily of oxytetracycline hydrochloride or chlortetracycline hydrochloride for 10 or 12 days. Individual doses of 0.75 to 1 gm. every 6 hours are advised. Late symptomatic syphilis, especially neurosyphilis and cardiovascular syphilis, should be treated with similar doses for at least 15 days. The Mayo Clinic achieved excellent results in the treatment of neurosyphilis with 50 to 90 gm. of chlortetracycline hydrochloride. In giving such large doses, every effort must be made to avoid gastrointestinal symptoms; however, antibiotics should always be preferred to treatment with arsenicals and bismuth. Despite the lack of conclusive data on the use of carbomycin, treatment might well be tried with 2 to 3 gm. of this antibiotic given daily for periods previously suggested.

Summary

A single treatment with 2,400,000 units of benzathine penicillin G can be used for the routine therapy of early and latent syphilis. If procaine penicillin G in oil and aluminum monostearate is used, routine therapy should consist of 4,800,000 units with individual injections of 1,200,000 units every 2 to 7 days. Valid data on the effects of treating late symptomatic syphilis, especially neurosyphilis and cardiovascular syphilis, with benzathine penicillin G are as yet unavailable, but three treatments with 2,400,000 units, with no more than 7 days intervening between each treatment, have been recommended. Good results in the treatment of late symptomatic syphilis have been obtained with total doses of 6 to 10 million units of procaine penicillin G in oil and aluminum monostearate. Individual doses of 1,200,000 units should be given two or three times a week. Patients with syphilis who are sensitive to penicillin can be treated with oxytetracycline hydrochloride, chlortetracycline hydrochloride, erythromycin, or carbomycin. Available data are confined to the first two. Minimal schedules with oxytetracycline hydrochloride or chlortetracycline hydrochloride consist of 3 to 4 gm. daily given in divided doses of 0.75 to 1 gm. every 6 hours for 10 to 12 days in early and latent syphilis and for at least 15 days in neurosyphilis and cardiovascular syphilis. Preliminary reports suggest that carbomycin in daily doses of 2 to 3 gm., for the same periods as advised above, may be effective.

COUNCIL ON FOODS AND NUTRITION

Report to the Council

The enrichment of flour and bread, recommended by the Food and Nutrition Board, National Research Council, and later recognized officially by the Federal Food and Drug Administration, follows certain policies that have long been advocated by the Council. In 1939, the Council announced that it would regard with favor the restorative addition of thiamine and certain other nutrients to white flour and bread. It therefore has been pleased to see the successful application of this policy in the rapidly extending use of enriched flour and enriched bread.

The following report is based on the remarks of Dr. Russell M. Wilder, a former member of the Council and the first chairman of the Food and Nutrition Board, at the dinner honoring Dr. R. R. Williams given by the American Institute of Baking at the Mayflower Hotel, Washington, D. C., April 23, 1956. The occasion recognized the 20th anniversary of the synthesis of thiamine by Dr. Williams and the 15th anniversary of the initiation of the enrichment program. The Council is pleased to authorize publication of this report.

Philip L. White, Sc.D., *Secretary.*

A BRIEF HISTORY OF THE ENRICHMENT OF FLOUR AND BREAD

Russell M. Wilder, M.D., Rochester, Minn.

The practice of making white flour by the process of roller milling was introduced about 1870. Although the texture and color of the white flour produced by this method was a great improvement over the gray, coarse, stone-ground flour, the more refined white flour contained much less of the coatings of the wheat grain and thus less vitamins and minerals. As a result of this process of milling and other changes in the preparation of our food, the amount of thiamine (vitamin B_1) and other so-called micronutrients was reduced in the American diet. From the first, there were critics of the roller-milling process, but after McCollum and Osborne and Mendel revealed the importance to health of these vitamins in the later 1910's, the flour millers and commercial bakers were under constant fire from physicians and nutritionists.

Reliable surveys of the nutritional condition of the people revealed that the average American diet of the 1930's contained only one-third the amount of thiamine as when stone-ground flour was the only flour available. This considerable reduction in the vitamin content of the diet and its deleterious effect on the public health led Dr. R. R. Williams of Bell Telephone Laboratories, New York, to say at a meeting of cereal chemists in New York City in 1939:

> All those are parts of the large problems which the carbohydrate industries face, that of making their staple products more nearly equivalent in nutritive value to the whole seed . . . as it was consumed by primitive man. Whether this is to be done by additions of synthetic materials or by retention of the original nutritive components of the crude food-stuffs is a question for industry to decide. To blink at the scientific facts which will presently become common knowledge, will be suicidal for the commercial enterprises concerned.

Actually, even before 1939 industry was attempting to find an answer to the need for nutritionally better flour and bread. It feared a return to the rough, gray flour of the past, diminished appeal of its products, and a further deceleration of the declining consumption of flour and bread. The persistent demand that all bread be made from wholewheat flour was of great concern to industry, knowing as it did that less than 3% of the buyers had ever found whole-wheat bread acceptable. Serious thought was being given to restitution to white flour of certain fractions removed in milling wheat. Attention was directed to the possibility of returning to the flour the delicate layer of skin of the covering of the wheat seed, the aleurone layer. This layer lies between the bran and the starchy interior of the seed and contains the major portion of the vitamins about which the nutritionists were concerned. In 1936 the synthesis of thiamine by R. R. Williams and J. K. Cline occurred, and it soon became commercially available.

Emeritus Member of the Mayo Clinic.

This was the situation in March, 1939, when the Council on Foods and Nutrition of the American Medical Association encouraged, with some qualifications, fortification of certain staple foods with vitamins and minerals, specifically the restorative additions of thiamine, niacin, riboflavin, iron, and calcium to white flour and white bread. Three events in the summer of 1940 quickened developments. First, the British government proposed to fortify flour with synthetic thiamine. Second, the recently appointed committee on medicine of the National Research Council advised reinforcement with thiamine of all white flour purchased for our military forces. Third, the Federal Food and Drug Administration scheduled public hearings to consider a standard of identity for flour. The recommendation of the committee on medicine was based on that of one of its subcommittees, which also had expressed itself on the need for a reinforced flour for the civilian population. The action of the Food and Drug Administration was in compliance with the new Food, Drug and Cosmetic Act, a law designed to strengthen the earlier food and drug law by setting standards for commodities. The procedure was, and is, to publish a proposed definition of a product and then to hold a public hearing to provide the opportunity for those opposed to the proposal to make known their objections.

TABLE 1.—*Levels of Enrichment for Varieties of Flour*

	Mg./Lb.	
	Minimum	Maximum
Thiamine	2.0	2.5
Riboflavin	1.2	1.5
Niacin	16.0	20.0
Iron	13.0	16.5
[illegible]	500	625
[illegible]	[illegible]	1,000 U.S.P. Units

* Required in self-rising flour, minimum, 500 mg., maximum, 1,500 mg. per lb. Optional in all enriched flours except self-rising.

† Optional

The proposal that was issued defined white flour as that flour which was in common use. This proposal, if adopted, would have closed the door to the improvements recommended by the committees. Physicians and scientists on those committees were disturbed, as were certain millers and bakers interested in and experimenting with the procedure recommended by the American Medical Association. Surgeon General Thomas Parran of the United States Public Health Service had been aroused by recently completed food-consumption surveys, particularly those of the Stiebeling-Phipard study from the Department of Agriculture. He and Dr. M. L. Wilson, director of the extension service, Department of Agriculture, who had recently been chosen to lead a nutrition committee within the government, were convinced that improvement of bread was basic to the effort demanded at that time to improve the nutrition of the people in the interest of national defense.

These hearings on flour were well attended. Many people wanted something done, but no agreement could be reached. Then the leaders of the industries involved met with the scientists concerned several times, and harmony of opinion was obtained for presentation when the hearings were resumed.

The Food and Nutrition Board was established as a part of the National Research Council to provide scientific guidance for the national nutrition program. It first assembled one week after the hearings on flour had been closed but before decisions had been reached. At this meeting the board endorsed the recommendations respecting flour that had been submitted to the Food and Drug Administration, and a committee on cereals was appointed to develop related standards for white bread. The American Bakers' Association and the American Institute of Baking assisted in the preparation of these standards. Finally, in March, 1941, at a meeting in Chicago to which all members of the baking and milling industries had been invited, and also at the National Nutrition Conference for Defense held in Washington in May, 1941, general endorsement of the enrichment program was obtained.

Tables 1 and 2 give the levels of enrichment for flour and bread, as finally stipulated in orders of the Federal Food and Drug Administration.

The levels set for bread are so related to those for flour that bread made from enriched flour will meet them. In actual practice the commercial baker frequently adds the enriching ingredients while making the dough.

Progress

Within a year, nearly all the large commercial bakers and major millers were voluntary enriching their white bread and family flour by adding thiamine, niacin, and iron. Preparations were being made to add riboflavin as soon as it could be made available. To promote the acceptance of these products by the public, pamphlets and posters were distributed by the millions; a major radio program entitled "Listen, America" was developed, and extensive advertising was conducted in newspapers and magazines. Assistance and encouragement came from many other quarters; the enrichment of flour and bread was endorsed by almost all professional organizations concerned in any way with public health. Orders issued by the Army and Navy made enrichment mandatory for flour that was purchased for their use. Promotion was extended by the nutrition councils of almost all the states, by the extension services of the federal and state governments, and by innumerable individuals, including physicians, dietitians, and home economists. Occasional but unimportant objections were raised to this program.

TABLE 2.—*Levels of Enrichment for Bread*

	Mg./Lb.	
	Minimum	Maximum
Thiamine	1.1	1.8
Riboflavin	0.7	1.6
Niacin	10.0	15.0
Iron	8.0	12.5
Calcium*	300	800
Vitamin D*	150	750 U.S.P. Units

* Optional.

In January, 1943, the first order issued by the newly created War Food Administration included a requirement that all baker's white bread be enriched. The war powers of the president ended with Japan's surrender, but in the meantime legislative action had been started at state levels. The legislature of South Carolina, on the urging of Dr. E. J. Lease and the state's nutrition council, was the first to take such action; the trend continued until 27 of the 48 states, as well as Puerto Rico and Hawaii, now have such legislation.

As a result of the personal efforts of Dr. Williams, the enrichment movement spread to other lands. Since more than three-fourths of the food calories in many countries come from cereals, the need for enrichment is even greater than in the United States. In the Orient, rice predominates in the diet, and it is also milled to whiteness. The preference of most consumers for white rice is insurmountable, and in torrid climates brown rice becomes rancid and infested quickly. Enrichment solves these problems, but the costs involved, small as they are, become significant in impoverished populations.

Enrichment of white flour was made compulsory in Newfoundland in 1944. The local government was so impressed with the benefits that continuation of the program was made a condition of annexation to Canada in 1949. Enrichment was prohibited in Canada at that time, but in 1953 the practice became permissible. The occasion was celebrated by a series of conferences across the Dominion. At the first of these, in Toronto, Dr. James McGrath, of the Ministry of Health of Newfoundland, made this comment: "Flour enrichment is still compulsory in Newfoundland. It is now permissible on a voluntary basis for the rest of Canada. . . . I will venture one prediction: that the benefits of enrichment are so evident that it will not be long before the use of enriched flour on a voluntary basis will be as extensive in the rest of Canada as it is now in Newfoundland where it is compulsory." This prediction has now become a reality.

During the war years in Great Britain, use of 85% extraction flour was compulsory. Later, the permissible extraction was lowered to 80%, meaning 80 parts of flour from every 100 parts of wheat. Use of 80% extraction flour is now encouraged by a subsidy, but white flour (72% extraction, or even less) can be sold; however, such low-extraction flour must be enriched with thiamine, niacin, and iron to the levels of 80% extraction flour. Not only are the levels lower than those in the enrichment formula used in the United States but there is no requirement for the addition of riboflavin. In Denmark, on the basis of conclusions reached by the Danish Academy for Technology, a government order was issued in December, 1953, requiring that all white flour, farina, and semolina offered for sale or delivery in Denmark contain 5 mg. of thiamine, 5 mg. of riboflavin, and 30 mg. of iron per kilogram of the respective material. In Sweden, most white flour is enriched with thiamine, riboflavin, niacin, and iron on a voluntary basis. In Germany and France there is practically no enrichment of flour or bread, but in Holland, Belgium, Switzerland, and Italy enrichment of flour is voluntary. In much of South America enrichment of wheat flour and other cereals is under discussion, but in Chile enrichment of all white flour has been mandatory for a year or more.

Benefit to Public Health

Those engaged in our enrichment program have repeatedly emphasized that the purpose of enrichment is to help correct certain defects in the diet. To make white bread a better food, desirable as that might be, is secondary to the use of flour and bread as vehicles for effecting an increased consumption of certain micronutrients. This has been accomplished. After enrichment of bread and flour became general, the average diet contained not only additional iron but almost twice the amount of thiamine, riboflavin, and niacin as before.

The enrichment program has played an important role in the disappearance of the frank deficiency diseases, beriberi and pellagra. For example, among 10,000 recent admissions to the Hillman General Hospital in Birmingham, Ala., not one patient with pellagra was found—this in an area in which pellagra previously had been rampant. At a large general hospital in Chicago, in which beriberi previously could always be observed, a 3-year search failed to reveal a single case of beriberi. In 1948 and 1949 a survey conducted among some 16,000 inmates of the Chicago House of Correction revealed only two cases of pellagra, three of ariboflavinosis, and no beriberi. A point of interest in this Chicago study was that the decline in the prevalence of these vitamin deficiency diseases started very shortly after the beginning of enrichment of bakery bread in Chicago. Between 1946 and 1950, a number of nutrition surveys were conducted in various areas of the country; surveys of family groups, of factory workers, of school children, and of others detected only an infrequent case of frank deficiency disease.

The benefits accruing from enrichment are by no means limited to prevention of the frank deficiency diseases. Some time ago I was engaged with others in extensive studies of the clinical effects of experimental diets low in thiamine. The studies yielded most convincing evidence that deficiency of this vitamin, to a degree insufficient to provoke frank beriberi, would produce disturbances of the psyche. Before enrichment was initiated, many diets in this country were low enough in thiamine to cause such effects. Even today, when enrichment of bread and flour is in general but not in universal use, a definite proportion of the people are probably subsisting on diets that are borderline in content of thiamine. To relax our efforts now would therefore be unfortunate.

A wealth of research and practical experience has proved the value of enriched bread in the diet of persons of a distinctly suboptimal nutritional status. Enriched bread is also believed to serve a purpose in diets that approach adequacy.

Although the enrichment program stemmed from the work of a great scientist, much credit for the success of the program should be given also to the pharmaceutical manufacturers of the micronutrients required. Tremendous quantities were called for at the lowest possible costs. These have been supplied at costs so low that the miller and commercial baker have been able to enrich their flour and bread at little or no additional expense to the consumer.

The flour and baking industries have voluntarily continued this program, whether or not state laws required it. Consequently, every person in this country is able to obtain this better bread, regardless of whether his residence is in one of the 27 states that make enrichment mandatory.

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION

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ANGINA PECTORIS—A THIRTY-YEAR PROGRESS REPORT

GUEST EDITORIAL

Arthur M. Master, M.D.

Only one generation ago, the diagnosis of "angina pectoris" was tantamount to the issuance of a death warrant. At that time, the severe, frequently excruciating pain that the patient suffered, the little understood prevention of the disease, and the condition's inadequate treatment engendered fears that could not reasonably be dispelled. In addition, cases of sudden death or severe heart attacks preceded by chest pain with normal three-lead electrocardiograms, i. e., no Q waves or RS-T segment elevations, were also considered episodes of angina pectoris. We now know that these were, for the most part, attacks of myocardial infarction due to complete obstruction of a coronary artery (occlusion) or bouts of prolonged severe myocardial ischemia without complete closure (coronary insufficiency). This added to the terror of the term angina pectoris. Today, in the light of recent advances and newer concepts in the prophylaxis of the disease and in its therapy, such an irrational approach to angina is not justified. Because the term angina pectoris is still so emotionally charged, however, it should be abandoned and a more descriptive, neutral label such as "chest pain due to coronary artery disease" should be employed.

The agonizing dread associated with the angina of 30 years ago was largely contributed to by the then existing economic and psychological factors. Social security, unemployment insurance, and adequate compensation laws had not as yet been enacted. Absence from work, for whatever reason, usually meant loss of pay. Mild attacks of angina, therefore, went unheeded. The sufferer necessarily continued on the job, simply for fear of losing it and his livelihood. Because both patients and doctors alike believed that the disease was clinically hopeless, early symptoms were often deliberately concealed from the family, the employer, and even the physician. When medical advice was finally sought, the condition was already full-blown. The late diagnosis of the majority of cases and the almost universal inadequacy of their treatment enhanced the general impression that angina pectoris was totally and permanently disabling. Undoubtedly the majority of patients given diagnoses and treated were in an advanced stage of their disease.

Only one generation ago, a definite diagnosis of angina pectoris was made only if the classic pattern of symptoms, described by Heberden in 1768, was present. It was necessary that the pain be crushing and vise-like in character and that it be associated with a "fear of impending death." It was necessary that the pain be substernal and that it radiate to the back, the jaw, or down the inner aspect of the left arm to the little and ring fingers. It was necessary that the pain invariably follow exertion, excitement, or emotion and that it be immediately relieved by amyl nitrite or glyceryl trinitrate (nitroglycerin). We now know that all these classic symptoms occur in only a minority of cases, and that any single one of them may be absent. Thus, severe coronary artery disease may produce only a dull ache. This may be precordial rather than substernal. The pain need not radiate down to the ulnar aspect of the hand. Indeed, it may not radiate at all from the site of its maximum intensity. It may not be precipitated by exertion; walking at even a good pace may not produce any discomfort. It may not be relieved by glyceryl trinitrate.

Formerly, a normal three-lead resting electrocardiogram was accepted as evidence that the chest pain was of noncardiac or psychogenic origin. Despite very suggestive clinical findings, the patient was frequently given a reassuring pat on the back and told not to worry. A subsequent heart attack occurred as a great surprise, especially to the physician, who attributed it to the natural vagaries of angina. Today, even a normal 12-lead resting electrocardiogram does not necessarily exclude the diagnosis of coronary artery disease, if the clinical history points to its presence. It is merely a reflection of the heart's ability to cope with the work load during the resting state. It is not an indication of the capability of the heart to meet the stress and strain of routine living. In an attempt to obtain this vital information, the Master two-step exercise test was devised.

When three or four of the characteristic features of angina, as described by Heberden, are present—the nature of the pain, its location, its radiation, and its precipitating factors—a diagnosis of a classic attack may usually be made. However, one or two of the features may be found in conditions other than coronary artery disease and may be absent in 10 to 40% of the cases of angina pectoris. An awareness of the possible variations of the clinical picture will make for more accurate diagnosis of coronary artery disease.

Thirty years ago, an anginal attack was treated with amyl nitrite perles. Often whiskey (spirituous liquors) was advised, because Heberden in 1768 had noted its soothing effect. Xanthines and theophylline were prescribed as coronary vasodilators, on the basis of experimental findings in the dog. Tobacco, even in small amounts, was taboo. Glyceryl trinitrate, for some unknown reason, was prescribed only when the pain was very severe, as if to suggest that its use signified the

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hopelessness of the condition. The usual dose was 1/100 grain (0.6 mg.), repeated frequently or until it relieved the pain.

The entire prophylactic, therapeutic, and psychological approach to angina has been much improved in recent years. Amyl nitrite is no longer routinely used in place of glyceryl trinitrate, because it produces a much more marked generalized vasodilation. The xanthines are not as frequently prescribed as formerly, having largely been replaced by coronary vasodilators such as pentaerythritol tetranitrate. There has been a major change in our use of glyceryl trinitrate; it is now employed not only in the treatment of the acute attack of angina but also in its prevention. Any pain-provoking stimulus that cannot be avoided is anticipated by the use of the drug prophylactically. When activities known to precipitate an anginal attack are undertaken —coitus, walking uphill, walking after a meal, walking early in the morning, stepping out into the cold, or walking against the wind—the patient is urged to take glyceryl trinitrate beforehand. Formerly, those who could afford it were encouraged to move to a warm climate. The intelligent use of glyceryl trinitrate prophylactically, however, usually obviates the need for such a move. The predictable prevention of anginal attacks eliminates much of the worry and despair formerly associated with the disease. The patient is more confident and the physician more optimistic, because both believe that angina pectoris is not a hopeless condition. Indeed, remissions do occur.

The dosage of glyceryl trinitrate is not as inflexible as it formerly was. Instead of the former routine 1/100 grain, the initial prescribed dose is often 1/200 grain (0.3 mg.) at present. Amounts even as small as 1/400 or 1/800 grain (0.15 or 0.075 mg.) may be effective. The dose required to relieve a particular patient is usually fairly constant; this dose may be repeated only once within a few minutes if the pain is not relieved by the first tablet. Should the second dose also be inefficacious, it may be wise to reevaluate the case lest acute coronary insufficiency or occlusion be overlooked, aggravated, or produced.

Formerly, as a last resort, patients with status anginosus were subjected to subtotal thyroidectomy. Today, similar effects may be obtained by the relatively innocuous administration of radioactive iodine. Occasionally, cardiopericardiopexy, internal mammary artery transplants, and other surgical procedures may yield good clinical results. Thirty years ago, these techniques were unknown. Stellate ganglion and thoracic sympathectomy or paravertebral blocks were attempted to secure relief from pain.

Tobacco is no longer banned in all cases. Its proscription depends on its effect on the patient's well-being. There is little point in forbidding a tense patient to smoke a little, if that serves to relax him. No longer is a patient allowed to drink excessively. If, however, one or two drinks a day serve to relax an otherwise apprehensive person, it would be unwise to prohibit them. Larger doses of alcohol actually overwork the heart and produce overweight. It was formerly thought that alcohol and tobacco in combination were good, since the former dilated the coronary vessels, which the latter constricted. This view is no longer accepted. It is now believed that a combination of alcohol and tobacco in less moderate doses actually aggravates the anginal syndrome.

Formerly, in patients with coronary artery disease, a major operation for some unrelated condition was considered to be very dangerous. All elective operations were barred by most cardiologists, and only last-resort procedures were permitted. Some of us have always advocated the removal of any focus of infection or irritation that may have a deleterious effect on the well-being of the patient with angina. A common example of the quandary in which physicians and surgeons found themselves was the problem of dealing with cholelithiasis. If gallstone colic developed, I have always recommended early extirpation of the gallbladder. Today, with the improved techniques in anesthesia and surgery, this attitude is more than ever justified. A state of anoxia is avoided, even for short periods, by the use of high concentrations of oxygen, by adequate pulmonary ventilation, by maintaining the blood pressure at an adequate level, and by promptly replacing the blood lost during the operation. As a result, patients with coronary artery disease tolerate surgical procedures extremely well.

Years ago, physicians hesitated to permit a patient with heart disease to fly. Today, however, with pressurized cabins and anti-motion-sickness drugs, there is no greater contraindication to flying than there is to use of any other form of transportation. Travel by airplane may even be preferable, since it obviates the long and often tiring trips by automobile, rail, and sea. The President's recent illness in Denver has again raised the question of whether persons with heart disease should live at high altitudes. I feel that most persons can "acclimatize" themselves to this environment after a period of time but that undue physical exertion should initially, at least, be avoided in an oxygen-poor atmosphere.

Despite all these improvements in therapy, the major change in the status of coronary artery disease in our age has been one of approach. While the pathophysiology is by no means completely understood, we now know that arteriosclerosis is not an inevitable process of aging. Timothy O'Leary, 20-odd years ago, found cholesterol abscesses in intimal plaques. Hence, a fat-poor diet was advocated as part of the treatment, but at that time little attention was given to this suggestion.

Today, it is realized that arteriosclerosis is a disease like any other. It is self-limited and, probably, a manifestation of some derangement of normal lipid metabolism. It may be affected by dietary and other factors. As a result, there has been an unparalleled surge of research in human and animal biochemistry. A renewed confidence has been born, as the result of a better understanding of arteriosclerosis and a hopeful approach to its prevention and cure. This has stimulated a more optimistic outlook among patients and physicians alike. Today, the designation "chest pain" or "coronary disease" is no longer a stigma. Its presence rightly generates caution, but not panic. Government and private agencies are making suitable jobs available for persons with arteriosclerotic heart disease.

The choice is no longer between working 60 hours a week or not at all. Jobs at lighter work, for 35 hours a week, or less, can now be found. The widespread interest and candid discussion of the President's recent coronary occlusion have made the condition further socially acceptable. Iatrogenic cardiophobia is on the wane. No longer is the patient—be he a well-known industrialist, a mill worker, or a doctor—reluctant to be seen in the consulting room of the cardiologist. The bank president or insurance executive no longer leaves by the back door of the doctor's office. To discuss one's electrocardiogram is as acceptable as to discuss one's analyst.

Until the ultimately inevitable specific prevention and treatment of coronary artery disease have been developed, general supportive measures remain of great importance. The patient who is overweight or obese is firmly advised to reduce. Ataraxics and sedatives are given to decrease tension. These measures, together with a confident outlook, will prolong the life of the patient. Thirty years hence, it is likely that enzymes, hormones, and other perhaps as yet unidentified biochemical agents will make angina pectoris a truly rare condition.

FIRST U. S. INTERNATIONAL MEDICAL FILM EXHIBITION

Each year the Film Library of the American Medical Association receives many unsolicited requests for medical films from physicians, medical societies, medical schools, and government agencies in various countries. Assistance is also requested in selecting top U. S. films to be shown abroad during international meetings of medical and scientific groups. It is evident that films from this country are in demand; and, conversely, we are anxious to see the results of medical advancements in other countries. What better way can this information be transmitted than by the use of a motion picture, which, along with its pictorial presentation, can carry explanations and comments by the man or men who did the work? Even without translation, medical and surgical films can speak an international language. Anatomy and physiology do not change at the border of a country. This comment was made following a recent medical meeting with international attendance: "It was good to see that, once more, 16-mm. films proved to be a unique medium for surmounting the language barriers that too often isolate professional workers attending congresses."

There is ample evidence to state that, first, the medical motion picture is an important force in communicating medical information at all levels; second, the arts and practices of medicine are global in their application and responsibility; and, third, the medical service, to which both of these apply, should be charged with the need to open all possible avenues to spread world wide the tools and techniques available to make the physical and emotional health of man the precursor to the ideal thought of as "the better world." But, in order to encourage and stimulate the flow of medical and scientific films on an international basis, the present import and export procedures must be simplified by government officials the world over. Some efforts have been made in this direction by UNESCO; and some countries, including the United States, are now thinking in terms of a customs simplification act. However, there is much more work to be done by all concerned if the barriers still existing to a practical exchange of such films are to be broken down further. Often numerous and complicated forms are required to secure the duty-free return of films that have been temporarily loaned to a colleague in another country. There are long delays and time-consuming procedures in clearing with customs—to say nothing of the expense in both time and money.

Why should not medical and scientific films, which are just another medium of communicating scientific information, be granted the same opportunity as books and printed materials to contribute to the education of physicians and surgeons in every country of the world?

This question along with others will be discussed at meetings scheduled to be held in connection with the International Film Exhibition. This exhibition, sponsored by the American Medical Association, in cooperation with Johnson & Johnson, will present an outstanding collection of foreign-made medical and surgical films as a special feature of the 106th Annual Meeting of the American Medical Association in New York, June, 1957.

Apart from the regular film theater, which will show the new and outstanding films produced in the United States, a theater will be devoted exclusively to the showing of these special films representing some of the outstanding medical research work being carried on in other countries. All films of distinction selected for showing will be translated and presented in English. This is the first time such a film presentation has been attempted in the United States.

In addition to the film exhibition, there will be ample opportunity for foreign guests and others interested to discuss the problems involved in the international exchange of medical films.

AID FOR HUNGARIANS

The Board of Trustees of the American Medical Association at its recent meeting in Seattle appropriated $5,000 to aid in the care of Hungarian refugees who are fleeing to Austria. The courage of these unfortunate people is known throughout the world, and to those who live in more fortunate countries it becomes a symbol for the men and women who believe enough in freedom to fight for it. Elsewhere in this issue of THE JOURNAL (page 1568) are two letters from the executive secretary of the American Medical Society of Vienna, a society known to physicians all over the world who have visited its headquarters. The executive secretary of the society has had, because of these responsibilities and others, a unique opportunity to see firsthand the plight of the fleeing people. He and his colleagues also through personal experience know the need for aid and how to meet the need during this time of urgency. Regardless of the size of the contribution it will be welcome.

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

SUPPLEMENTARY LIST–CORRECTIONS

In the annual Internship and Residency Number of The Journal, Sept. 22, 1956, incomplete or inaccurate data were presented. The corrected entries are as follows:

APPROVED RESIDENCIES AND FELLOWSHIPS

ANESTHESIOLOGY

Name of Hospital	Chief of Service	Total Anesthetics	Inhalation Anesthetics	First Year Residencies Offered*	Total Residencies Offered*	Beginning Stipend (Month)
Bronx Municipal Hospital Center [1-3], New York City	L. R Orkin	103	70	10	21	$105

DERMATOLOGY AND SYPHILOLOGY

Name of Hospital	Chief of Service	Inpatients Treated	Outpatient Visits	First Year Residencies Offered*	Total Residencies Offered*	Length of Approved Program (Years)	Beginning Stipend (Month)
University of California Hospital [1-3] San Francisco	R. B. Rees, Jr	46	7,154	2	4	3	200

INTERNAL MEDICINE

Name of Hospital	Chief of Service	Inpatients Treated	Autopsies	First Year Residencies Offered*	Total Residencies Offered*	Length of Approved Program (Years)	Beginning Stipend (Month)
Beekman-Downtown Hospital [1], New York City	M. McCall	1,651	80	2	2	1	190

NEUROLOGY

Name of Hospital	Chief of Service	Inpatients Treated	Autopsies	First Year Residencies Offered*	Total Residencies Offered*	Length of Approved Program (Years)	Beginning Stipend (Month)
University of Louisville Affiliated Hospitals						3	
Louisville General Hospital [1-3] Louisville, Ky.	E. Roseman	728	55	1	3	..	131
Veterans Administration Hospital [1-3], Louisville, Ky.	I. O. Dien	281	10	1	1	..	...
Duke University Hospital [1-3], Durham, N. C.	E. C. Kunkle	241	1	2	5	3	102

ORTHOPEDIC SURGERY

Name of Hospital	Chief of Service	Type of Training	Inpatients Treated	Autopsies	First Year Residencies Offered*	Total Residencies Offered*	Program Identification	Beginning Stipend Offered*
Mississippi Baptist Hospital [1] Jackson, Miss	T. H. Blake	ACF	1,566	3	1	3	73	150
University of Mississippi Medical Center								
University Hospital, Jackson, Miss.	W. F. Enneking	AF	...	...	...	...	73	...
Veterans Administration Hospital, Jackson, Miss.	W. F. Enneking	AF	...	...	...	...	73	...
Pittsburgh Medical Center								
Children's Hospital [1-3] Pittsburgh	A. B. Ferguson, Jr.	C	603	...	3	5	6, 30	125
Presbyterian Hospital Pittsburgh	A. B. Ferguson, Jr.	AF	554	2	...	3	30	125
Veterans Administration Hospital [1] Pittsburgh	A. B. Ferguson, Jr.	AF	...	10	...	2	30	...

OTOLARYNGOLOGY

Name of Hospital	Chief of Service	Inpatients Treated	Outpatient Visits	First Year Residencies Offered*	Total Residencies Offered*	Length of Approved Program (Years)	Beginning Stipend (Month)
Baylor University Coll. of Medicine Affiliated Hospitals						3	
Jefferson Davis Hospital [1-3] Houston, Texas	H. H. Harris	250	7,033	1	2	..	75
Methodist Hospital [1-3], Houston, Texas	J. C. Dickson	754	....	1	1	..	220
Veterans Administration Hospital Houston, Texas	....	390	....	1	3	..	...

PATHOLOGY

Name of Hospital	Chief of Service	Number of Autopsies	Number of Surgical Specimens	Number Examined Microscopically	Total Number of Laboratory Examinations	First Year Residencies Offered*	Total Residencies Offered*	Length of Approved Program (Years)	Beginning Stipend (Month)
U.S. Naval Hospital [1] San Diego, Calif.	J. S. Shaver	475	7,401	7,401	594,152	2	5	4^{P}	...
Medical College of Virginia, Hospital Division [1-3] Richmond, Va.	F. L Apperly, H. G. Kupfer	536	9,506	9,006	544,405	...	9	4^{P}	75

PEDIATRICS

Name of Hospital	Chief of Service	Inpatients Treated	Autopsies	First Year Residencies Offered*	Total Residencies Offered*	Length of Approved Program (Years)	Beginning Stipend (Month)
Grace-New Haven Community Hospital [1-3-69], New Haven, Conn.	M. J. E. Senn, W. R. Wilson	5,341	83	6	10	2	50
St. John's Hospital [1-3], Tulsa, Okla.	G. R. Russell	3,791	16	2	8	2	175

PSYCHIATRY

Name of Hospital	Chief of Service	Inpatients Treated	Autopsies	First Year Residencies Offered [8]	Total Residencies Offered [8]	Length of Approved Program (Years)	Beginning Stipend (Month)
Mississippi State Hospital [1], Whitfield, Miss.	J. J. Head....	7,714	76	6	6	1	300

THORACIC SURGERY

Name of Hospital	Chief of Service	Inpatients Treated	Autopsies	First Year Residencies Offered [8]	Total Residencies Offered [8]	Beginning Stipend (Month)
Vanderbilt University Hospital [1-3], Nashville, Tenn.	R. A. Daniel, Jr.	231	12	...	1	50

UROLOGY

Name of Hospital	Chief of Service	Inpatients Treated	Autopsies	First Year Residencies Offered [8]	Total Residencies Offered [8]	Length of Approved Program (Years)	Beginning Stipend (Month)
Francis Delafield Hospital [1-3], New York City	J. K. Lattimer	269	27	4	7	3	106
Charlotte Memorial Hospital [1] Charlotte, N. C. ...	H. McKay	1,413	10	1	4	3	270

HOSPITALS APPROVED FOR RESIDENCY TRAINING

The following hospitals should be listed under "Hospitals Approved for Residency Training" as follows:

Butterworth Hospital * Grand Rapids, Mich..	Anes., Int. Med., Ob.-Gyn., Path., Ped., Rad., Surg
Sacred Heart Hospital * Spokane, Wash.	*Gen'l Pract., Ob.-Gyn., Path., Rad., Surg.*

BUREAU OF MEDICAL ECONOMIC RESEARCH

SOME CATEGORIES OF PATIENTS TREATED BY PHYSICIANS IN HOSPITALS

Frank G. Dickinson, Ph.D.
and
James Raymond, M.A., Chicago

The Bureau of Medical Economic Research of the American Medical Association has a number of studies under way that are designed to produce an estimate of the totality of services rendered by physicians to the American people annually.[1] The first item in this series presented data on the age and sex distribution of patients treated by physicians in hospitals; the excess of male patients in the hospitals in the United States on a given day was surprising.[2] The present study considers hospital patients only in selected categories chosen because each includes a large number of patients and because it was reasonable to expect that hospital administrators and medical record librarians could furnish the necessary data for the entire year of 1954. We wish to express our deep appreciation to the hospital administrators, the medical record librarians, and other hospital staff members for their cooperation in a difficult undertaking. The next study will deal with the role of accidents in the services of physicians to their hospitalized patients. Subsequent studies in the series will involve estimates of the numbers of patients seen by physicians in the home and in the office as well as of patients in all diagnostic groups seen during a selected week in all hospitals. When this series is completed several years hence, the Bureau will have presented a rough estimate of the totality of the services rendered annually by physicians to the American people. It will then be possible for the first time to present a counterpart to the total expenditures of the people for medical care—the value side as well as the cost side of physicians' services. In other words, this series of studies is designed to describe what we get in terms of ailments treated for what we spend for physicians' service.

Moreover, these studies should provide much additional information on morbidity, for which nationwide data are deficient in both quality and quantity. Measures of the volume of medical care—other than dollar totals—and its components are incomplete in many fields. For instance, although information is available on the contagious diseases for the nation as a whole, there are only sampling studies of total morbidity for selected areas, and these are for limited periods of time.[3] Thus, the available national data on the contagious diseases demonstrate a highly significant decline in the incidence of diphtheria and scarlet fever in the last 25 years, but the decline in the number of mastoid operations performed by physicians, well known to older members of the profession, is not similarly demonstrable through statistical measures. This lack of comparative morbidity data and of quantified data on operations and other treatments presents many difficulties to those who would compare the past with the present in order to plan for future developments in the field of medical care, including methods of budgeting and payment.

Organization and Scope of Study

So many complications have developed in the preparation of this report, as well as in the survey itself, that it seems wise to present two reports. This article will be reprinted without additions from THE JOURNAL as Bulletin 102 of the Bureau of Medical Economic

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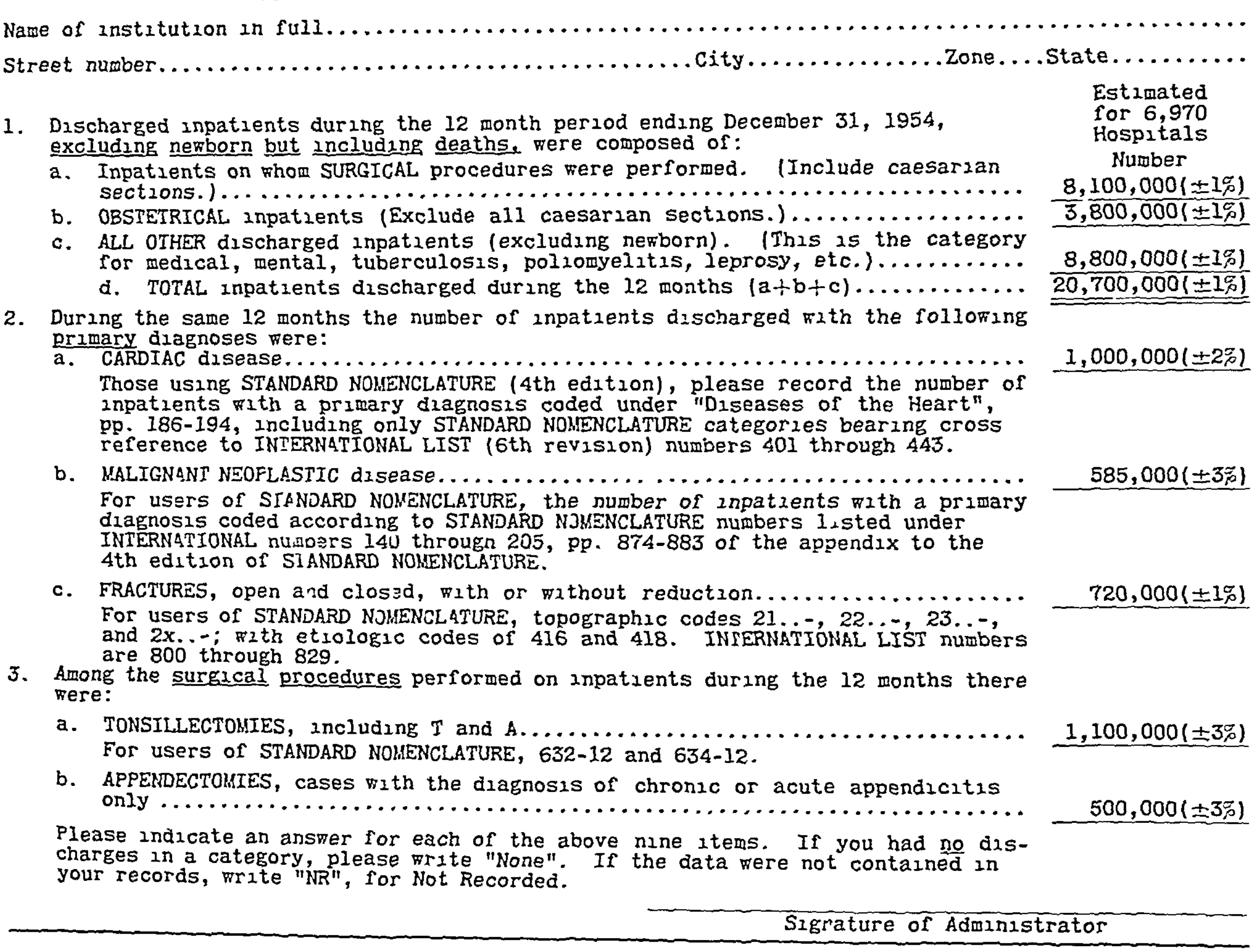
Director (Dr. Dickinson) and Staff Associate (Mr. Raymond), Bureau of Medical Economic Research, American Medical Association.

Research. Its companion, Bulletin 102A, supplement to Bulletin 102, will contain the appendix tables not presented herein and some discussions of alternate procedures for making national estimates. The two items will probably be bound together.

It was early determined that the scope of the present study would be restricted to hospital inpatients classified according to some of the most common diagnostic categories of inpatients discharged from 6,970 hospitals accepted for listing by the American Hospital Association in 1954. The rather general and, hence, limited scope of the study is most succinctly circumscribed by an examination of the survey questionnaire and of the results obtained, both of which are presented in the chart

CHART 1.—*Estimated Data (Rounded) for 6,970 Hospitals Accepted for Listing by the A H A. in 1954*



SECTION III--STATISTICAL STUDY--AMERICAN MEDICAL ASSOCIATION

Name of institution in full...

Street number...City................Zone....State...........

	Estimated for 6,970 Hospitals Number
1. Discharged inpatients during the 12 month period ending December 31, 1954, excluding newborn but including deaths, were composed of:	
a. Inpatients on whom SURGICAL procedures were performed. (Include caesarian sections.)........	8,100,000(±1%)
b. OBSTETRICAL inpatients (Exclude all caesarian sections.)........	3,800,000(±1%)
c. ALL OTHER discharged inpatients (excluding newborn). (This is the category for medical, mental, tuberculosis, poliomyelitis, leprosy, etc.)........	8,800,000(±1%)
d. TOTAL inpatients discharged during the 12 months (a+b+c)........	20,700,000(±1%)
2. During the same 12 months the number of inpatients discharged with the following primary diagnoses were:	
a. CARDIAC disease........	1,000,000(±2%)
Those using STANDARD NOMENCLATURE (4th edition), please record the number of inpatients with a primary diagnosis coded under "Diseases of the Heart", pp. 186-194, including only STANDARD NOMENCLATURE categories bearing cross reference to INTERNATIONAL LIST (6th revision) numbers 401 through 443.	
b. MALIGNANT NEOPLASTIC disease........	585,000(±3%)
For users of STANDARD NOMENCLATURE, the number of inpatients with a primary diagnosis coded according to STANDARD NOMENCLATURE numbers listed under INTERNATIONAL numbers 140 through 205, pp. 874-883 of the appendix to the 4th edition of STANDARD NOMENCLATURE.	
c. FRACTURES, open and closed, with or without reduction........	720,000(±1%)
For users of STANDARD NOMENCLATURE, topographic codes 21..-, 22..-, 23..-, and 2x..-; with etiologic codes of 416 and 418. INTERNATIONAL LIST numbers are 800 through 829.	
3. Among the surgical procedures performed on inpatients during the 12 months there were:	
a. TONSILLECTOMIES, including T and A........	1,100,000(±3%)
For users of STANDARD NOMENCLATURE, 632-12 and 634-12.	
b. APPENDECTOMIES, cases with the diagnosis of chronic or acute appendicitis only........	500,000(±3%)

Please indicate an answer for each of the above nine items. If you had no discharges in a category, please write "None". If the data were not contained in your records, write "NR", for Not Recorded.

Signature of Administrator

The chart is a copy of the survey questionnaire with approximate totals for all hospitals inserted in the answer spaces. After a discussion of the chart the remainder of this article is largely devoted to the replies received and estimates for the hospitals that did not reply.

Estimated Totals for the 6,970 Hospitals

As indicated by the title, "SECTION III—STATISTICAL STUDY—AMERICAN MEDICAL ASSOCIATION," this schedule was a part of the joint A. M. A. and A. H. A. survey of hospitals for 1954. Other results of this joint survey have been reported in two parts.[4] It will be at once noted from the questions asked in this study that yearly totals of discharged inpatients in certain diagnostic categories were called for; information was not requested on the age, sex, or length of stay of these inpatients nor on the number and variety of specific procedures performed on them by their physicians while they were in the hospital. The totals presented in the chart are approximations, the plus-or-minus variation is indicated after each total. They are approximations because not all of the 6,970 hospitals accepted for listing in 1954 by the A. H. A. replied to this particular questionnaire in whole or in part, making it necessary for estimates to be made for the nonreplying hospitals Moreover, the two operative procedures specified were rarely performed in certain specialized types of hospitals such as the 596 nervous and mental and 393 tuberculosis hospitals.

Question 1.—The first question was designed to obtain the number of inpatients discharged during the calendar year 1954, excluding newborn infants but including patients who died. The total number of inpatients discharged is set forth in *1d* of the chart as the sum parts of *a*, *b*, and *c*; discharged inpatients treated by physicians in hospitals during calendar year 1954 totaled 20,700,000 (± 1%). The admissions to these same hospitals reported by the A. H. A. for the 12 months ending Sept. 30, 1954, totaled 20,345,000 pitals within that category. Third, when the number of discharges reported by the replying hospitals in any subcategory was treated as a percentage of total discharges given by the replying hospitals, the resulting percentage pattern was almost exactly the same as that for admissions to the replying hospitals [col. (7) compared with, col. (4)]; the greatest variation was 0.1 percentage point. Variations in admissions and discharges were similar, and, as noted, they were of similar magnitude. Fourth, the discharges reported by all replying hospitals were 1.5 percentage points, or 240,592, more than the admissions to the same hospitals [see col. (8)]. For only the general and special hospitals the discharges were 1.7 percentage points (258,944) in excess of their admissions; discharges from the mental and tuberculosis hospitals were 6.3 percentage points (18,352) fewer than their number of admissions.

Some small fraction of the excess may be due to the fact that the reporting period for discharges includes three more recent months than the A. H. A. reporting period for admissions. While available data show a clear tendency for the number of hospital admissions to rise over a period of several years, the data do not permit the calculation of any very reliable monthly rate of increase; this is because the number of reporting hospitals has varied each year and because even those hospitals that have reported consistently have been subject to local fluctuations and changes in the demand for their service. It is probable that some of the 1.5% excess of discharges over admissions is due to reporting errors of several varieties. In the editing of the returned questionnaires, a check of the number of discharges reported by each hospital against the number of admissions reported to the A. H. A. was made; when the two figures differed by 20% or more, letters of inquiry obtained many replies to the effect that the hospitals had failed to exclude newborn infants, as directed, from the count of discharged patients. Very probably there were other hospitals for which the figures differed less than 20% that also failed to exclude newborn infants, but we gave them no opportunity to correct their reporting error. Other hospitals stipulated that the number of discharges reported to the Bureau was correct but that the number of admissions reported to the A. H. A. was in error. The cumulation of these and other errors may account for some of the difference.

The fact that admissions and discharges matched as closely as they did is of major significance for this study. For the general and special hospitals at least, we are justified in regarding admissions and discharges as being of practically the same magnitude. Moreover, the mental and tuberculosis hospitals had only 1.9% of the admissions and only 1.7% of the discharges reported upon here. There is, therefore, little reason to believe that the percentages of discharges for each section of the questionnaire, reported in the following paragraphs, are distorted by the use of number of discharges, rather than admissions, as a base.

Estimates for Nonreplying Hospitals

Because some groups of hospitals did not reply in the same proportion as the total, 62.1% of all replying hospitals, it was concluded that estimates should be based upon that factor wherein the greatest amount of representativeness was obtained—undoubtedly admissions (76.5%)—and that estimates should be made for as many different classes of hospitals as possible. Accordingly, estimates were prepared for each of the 11 classes of hospitals shown in tables 1 and 2 (11, because there are no mental and tuberculosis hospitals in the subcategory "Federal-Military") based on the ratios of the number of admissions in the nonreplying hospitals to the number of admissions in the replying hospitals. A second set of computations utilized the ratios of number of beds, and a third set was based on these ratios for average daily census. Primarily because the estimates based on numbers of admissions gave an estimated total number of discharges from all 6,970 hospitals that varied by the smallest amount from the known numbers of admissions to these hospitals, these are the estimates reported here. The estimates appearing in the chart are based primarily on admissions, and the range above and below the number entered indicated by the percentage in parenthesis is broad enough, in most cases, to encompass the higher and lower estimates based on beds and average daily census. Appendix tables show the somewhat larger estimates resulting when the

TABLE 2.—*Comparison of Admissions and Discharges, by Hospital Type of Service and Type of Control, 1954*

Type of Service and Type of Control	Admissions to All Hospitals		Admissions to Replying Hospitals			Discharges from Replying Hospitals		
	No (1)	% (2)	No (3)	% (4)	% of Admissions [(3)÷(1)] (5)	No (6)	% (7)	% of Admissions [(6)÷(3)] (8)
General and special								
Nongovernmental	14,895,208	73.2	11,556,619	74.3	77.6	11,754,762	74.4	101.7
Local government	3,126,269	15.4	2,354,013	15.1	75.3	2,407,535	15.2	102.3
State government	525,323	2.6	380,503	2.4	72.4	389,075	2.5	102.3
Federal government	1,352,576	6.6	988,213	6.3	73.1	986,950	6.2	99.9
Military	(813,868)	(4.0)	(550,531)	(3.5)	(67.6)	(557,033)	(3.5)	101.2
V.A.	(431,674)	(2.1)	(354,298)	(2.3)	(82.1)	(344,848)	(2.2)	97.3
Other	(107,014)	(0.5)	(83,384)	(0.5)	(77.9)	(85,069)	(0.5)	102.0
(Subtotal)	19,899,446	97.8	15,279,378	98.1	76.8	15,538,322	98.3	101.7
Mental and tuberculosis*								
Nongovernmental	97,265	0.5	60,361	0.4	62.1	58,879	0.4	97.5
Local government	48,971	0.2	35,769	0.2	73.0	34,903	0.2	97.6
State government	231,789	1.1	138,273	0.9	59.7	125,790	0.8	91.0
Federal government	67,969	0.4	55,711	0.4	82.0	52,190	0.3	93.7
V.A.	(57,233)	(0.3)	(50,601)	(0.3)	88.4	47,033	0.3	92.9
Other	(10,727)	(0.1)	(5,110)	(0.1)	47.6	5,157	*	100.9
(Subtotal)	445,985	2.2	290,114	1.9	65.0	271,762	1.7	93.7
Total	20,345,431	100.0	15,569,492	100.0	76.5	15,810,084	100.0	101.5

* No military hospitals in this category

hospitals were classified according to size or regional location and when the rates for number of beds and/or average daily census were used. We definitely prefer the estimates based on admissions.

Four different ratios were computed and used in estimating the numbers for the nonreplying hospitals in question 2 and 3. This was necessary because not every one of the 4,329 hospitals that answered question 1 replied to all parts of questions 2 and 3. Indeed, it was not expected that question 2—dealing with discharged inpatients having the primary diagnoses of cardiac disease, malignant neoplastic disease, or fractures—would be applicable to the mental and tuberculosis hospitals; so the basis of estimation here became the number of admissions to only the six groupings of the 5,981 general and special hospitals. There were 2,909 general and special hospitals that answered part *a* of question 2 (cardiac disease), 2,961 that answered part *b* (malignant neoplastic disease) and 3,227 that answered part *c* (fractures). This meant that three different sets of ratios of admissions in nonreplying to replying hospitals had to be computed. As for question 3, the numbers of tonsillectomies and appendectomies performed in the replying mental and tuberculosis hospitals were, while not large, of sufficient size to warrant the consideration of this question as applicable to all hospitals and, hence, to permit estimation of nonreplies on the basis of the total admissions to all 6,970 hospitals. There were 570 mental and tuberculosis hospitals among the 4,088 hospitals that gave usable answers to question 3.

Three Groups of Inpatients Discharged

The replying hospitals reported that they discharged 15,810,084 inpatients during 1954; 271,762 were from mental and tuberculosis hospitals. Inpatients on whom physicians performed some surgical procedures numbered 6,238,660 of these discharges; through projection this number was raised to 8,106,134 (rounded to 8,100,000 on the chart) for all hospitals accepted for listing by the A. H. A. in 1954. The replying hospitals reported 2,902,865 inpatients classified as obstetric among their total discharges for the year, and it was estimated that 884,322 more such patients were discharged from the nonreplying hospitals; thus the projected total was 3,787,187 obstetric inpatients discharged (rounded to 3,800,000 on the chart) for the year. The A. H. A. census reported 3,342,599 births in 4,869 hospitals during the year ending Sept. 30, 1954. Only 5,800 of the reported obstetric patients were from mental and tuberculosis hospitals; and the estimated total for all mental and tuberculosis hospitals was only 7,979. (Of the 5,666 obstetric discharges reported by local government hospitals in the mental and tuberculosis category, 5,644 were reported by Herman Kiefer Hospital in Detroit (east north central region). This hospital, coded as a tuberculosis hospital on the A. H. A. punch cards, has large maternity and isolation sections. The A. H. A. data on this hospital for the year ending Sept. 30, 1954, are 1,450 beds, 8,636 admissions, 1,118 average daily census, and 4,855 births. This hospital reported, for the year ending Dec. 31, 1954, 1,594 surgical, 5,644 obstetric, 1,345 "other," and a total of 8,583 discharges, plus 3 tonsillectomies and 9 appendectomies.) The total reported for the third group, "All other" (part *c*, question 1), was 6,668,559 discharges; the total reported for the three groups was 15,810,084 discharges. The "All other" cases were increased to 8,762,106 (rounded to 8,800,000 on the chart) when the estimates for the nonreplying hospitals were included; and the total estimated inpatient hospital discharges for the calendar year 1954 was 20,655,427 (rounded to 20,700,000 on the chart). The results of the survey, together with the estimates for the nonreplying hospitals, are shown in table 3. This summary is derived from appendix tables, some of which show the computations of estimates for the nonreplying hospitals.

Of somewhat greater interest than mere numbers are percentages of all discharges accounted for in each diagnostic category—parts *a*, *b*, and *c* of questions 1 and 2 and parts *a* and *b* of question 3. These percentages were obtained by dividing the reported number of inpatients in a diagnostic category by the reported total inpatients discharged from the hospitals that answered that particular question. (The replies to each item in the questionnaire from the general and special and from the mental and tuberculosis hospitals, their total discharges, and the resulting percentages, are shown in table 4.) Inpatients upon whom their physicians performed some surgical procedures were nearly two-fifths (39.4%) of the inpatients discharged from all replying hospitals. Obstetric patients were 18.4% of the reported discharges—somewhat higher than a previous estimate of around 17.5% (Bulletin 99 [6]), and the remaining 42.2% were, of course, inpatients in the "All other" category. The replying mental and tuberculosis hospitals as a group discharged only 271,762 of the nearly 16 million total reported discharges. When the estimates for the 382 nonreplying mental and tuberculosis hospitals were included, these discharges were only 417,549 inpatients out of the nearly 20,700,000 discharged during the year. Exclusion of these two types of hospitals made the percentages of inpatients discharged from the general and special hospitals only slightly different (40 for surgical, 18.6 for obstetric, and 41.4 for "All other") from the percentages for all the hospitals cited above. The percentages for the mental and tuberculosis hospitals treated as a group were, however, quite different; 86.8% of the discharges were in the "All other" category, while only 11.1% were classified as surgical; obstetric cases were 2.1% and would have been about 0.1% if the one tuberculosis hospital (with many nontuberculous inpatients) had not been included.

While the term "surgical cases" was not defined rigorously enough to permit detailed analysis of such discharges, it may be significant that four-fifths of all reported surgical patients discharged were from the nongovernmental general and special hospitals. Of the obstetric discharges, 99.8% were from general and special hospitals. In fact, all but 156 of the reported obstetric discharges would have been included in this group if one hospital with large maternity and isolation sections had not been coded as a tuberculosis hospital. Even though most of the discharges from mental and tuberculosis hospitals were in the "All other" category, they were only 3.5% of all discharges in the "All other" category. These percentages are derived from the data given in table 3; complete percentage distributions appear in the appendix.

As shown in table 2, the total inpatients discharged from mental and tuberculosis hospitals constituted only 1.7% of all reported (15,810,084) inpatients discharged for the year. Most of the remaining comments are, therefore, concerned with the 98.3% of the inpatients discharged from the general and special hospitals.

Table 4 shows the percentage distribution by categories of all reported inpatients discharged by the general and special hospitals classified according to type of control. The percentages in column (1)—for all replying general and special hospitals—vary considerably from the percentages in the same row in the other columns. For example, although 40% of the reported inpatients discharged from all general and special hospitals were surgical discharges [col. (1)] the range was 27.4% from military hospitals to 42.5% from nongovernmental hospitals. The percentage distribution for obstetric discharges is almost incredible—18.6% for all hospitals, with a high of 19.5% from federal military hospitals (108,584 out of 557,033 inpatients discharged). Bearing in mind the fact that our general objective in this five-year study is to measure the totality of physician services, we feel constrained to ask a sharp question: Why should physicians have a larger proportion of obstetric patients (discharged) in military hospitals than in nongovernmental or local governmental hospitals in the general and special class of hospitals?

Size of Hospital.—Appendix tables in Bulletin 102A show some rather interesting variations when the replying general and special hospitals are grouped according to size. The largest number of each of the three types (1*a*, 1*b*, and 1*c*) of discharges was from hospitals having 100 to 199 beds. The ratio of surgical discharges to all discharges was largest (44.3%) for hospitals in the bed-size class 300 to 499. Large general and special hospitals, those having 500 or more beds, accounted for the smallest proportion of obstetric cases, 16.5%; the proportion was highest, 19.5%, in hospitals having fewer than 25 beds. As noted in the appendix, the highest estimate for nonreplying hospitals was based on a classification of hospitals by size.

Hospital by Region.—Other appendix tables reveal that the largest number of each group of discharges was made from hospitals in the east north central region. As might be expected from the regional birth rates, the ratio of obstetric cases to all discharges was also highest (20.1%) for the east north central region and lowest (17.5%) for hospitals in New England. Estimates for the nonreplying hospitals, when made by region, did not vary by more than a few thousand from those made on the basis of type of control.

TABLE 3.—*Basic Data from Replying Hospitals, Estimates for Nonreplying Hospitals, and Estimated Totals for all Hospitals, 1954*

	Replying Hospitals				Nonreplying Hospitals		All Hospitals	
Hospital Type of Service and Diagnostic Category of Discharged Patients	No. (1)	Inpatients in Diagnostic Category, No. (2)	Total Discharges from These Hospitals (3)	Discharges, % [(2)÷(3)] (4)	No. (5)	Inpatients, Estimated No. (6)	No. [(1)+(5)] (7)	Inpatients, Estimated No. [(2)+(6)] (8)
General and special hospitals								
1*a*. Surgical	3,722	6,208,615	15,538,322	40.0	2,259	1,855,428	5,981	8,064,043
b. Obstetric	3,722	2,897,065	15,538,322	18.6	2,259	882,143	5,981	3,779,208
c. "All others"	3,722	6,432,642	15,538,322	41.4	2,259	1,961,985	5,981	8,394,627
(Subtotal)	3,722	15,538,322	15,538,322	100.0	2,259	4,699,556	5,981	20,237,878
Mental and tuberculosis hospitals								
1*a*. Surgical	607	30,045	271,762	11.1	382	12,046	989	42,091
b. Obstetric	607	5,800	271,762	2.1	382	2,179	989	7,979
c. "All others"	607	235,917	271,762	86.8	382	131,562	989	367,479
(Subtotal)	607	271,762	271,762	100.0	382	145,787	989	417,549
1*a*. Surgical subtotal	4,329	6,238,660	15,810,084	39.4	2,641	1,867,474	6,970	8,106,134
b. Obstetric subtotal	4,329	2,902,865	15,810,084	18.4	2,641	884,322	6,970	3,787,187
c. "All others" subtotal	4,329	6,668,559	15,810,084	42.2	2,641	2,093,547	6,970	8,762,106
1*d*. Total		15,810,084	15,810,084	100.0	2,641	4,845,343	6,970	20,655,427
General and special hospitals only								
2*a*. Cardiac	2,909	627,168	12,776,529	4.9	3,072	362,484	5,981	989,652
b. Malignant neoplasm	2,961	396,320	13,283,572	3.0	3,020	205,296	5,981	601,616
c. Fracture	3,227	501,629	14,092,233	3.6	2,754	219,662	5,981	721,291
General and special hospitals								
3*a*. Tonsillectomy	3,518	812,244	14,893,787	5.5	2,463	287,744	5,981	1,099,988
b. Appendectomy	3,518	357,316	14,893,787	2.4	2,463	127,397	5,981	484,713
Mental and tuberculosis hospitals								
3*a*. Tonsillectomy	570	895	255,964	0.3	419	582	989	1,477
b. Appendectomy	570	832	255,964	0.3	419	417	989	1,249
3*a*. Total—tonsillectomy	4,088	813,139	15,149,751	5.4	2,882	288,326	6,970	1,101,465
b. Total—appendectomy	4,088	358,148	15,149,751	2.4	2,882	127,814	6,970	485,962

Cardiac and Neoplastic Disease and Fractures

It is important to emphasize the fact that the data presented in the survey do not account for all patients with a diagnosis of cardiac or neoplastic disease or fractures who were treated by physicians in hospitals in 1954. Undoubtedly there were large numbers of discharged inpatients with each of these conditions as secondary diagnoses. Because primary diagnoses were called for, the cardiac and neoplastic diseases and fractures were not among the primary diagnoses reported by the mental and tuberculosis hospitals. Moreover, since every general and special hospital in the survey did not answer all three parts of question 2, percentages of all discharges are based upon the discharges reported by the hospitals that did reply to the particular item, including those that reported "none." (Replies for each subcategory of replying hospitals, together with the estimated total for all hospitals, are shown in the appendix tables.)

As table 3 shows, the 2,909 replying general and special hospitals reported 627,168 inpatients having a primary diagnosis of cardiac disease discharged during the calendar year 1954. It is estimated that the nonreplying 3,072 general and special hospitals, which had only 37% of the admissions, discharged an additional 362,484 such patients during the same period, bringing the estimated total for all 5,981 general and special hospitals to 989,652. This is rounded to 1 million on the chart. Discharged inpatients with a primary diagnosis of cardiac disease were 4.9% of the number discharged from general and special hospitals. Interestingly enough, the highest percentage, 11.7, was from Veterans Administration hospitals; the percentage for local governmental hospitals was also higher than for the total (see table 4).

The 2,961 hospitals that answered the question on inpatients discharged with a primary diagnosis of malignant neoplastic disease reported 396,320 such patients. It is estimated that the 3,020 nonreplying hospitals discharged 205,296 such patients, bringing the total for all general and special hospitals to 601,616. This is reduced to 585,000 on the chart because of the lower estimate (571,000) based on admissions by size.

Table 4.—*Percentage Distribution by Eight Categories of Reported Inpatients Discharged from General and Special Hospitals, According to Hospital Type of Control, 1954*

Diagnostic Category of Discharged Inpatients	All (1)	Non governmental (2)	Local Government (3)	State Government (4)	Federal Government Total (5)	Federal Government Military (6)	Federal Government V. A. (7)	Federal Government Other (8)
1 a Surgical	40.0	42.5	31.0	37.7	32.0	27.4	39.3	33.1
b. Obstetric	18.6	19.1	19.3	18.2	11.9	19.5	0.0	10.2
c "All others"	41.4	38.4	49.7	44.1	56.1	53.1	60.7	56.7
d Total	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
2 a Cardiac	4.9	4.7	5.7	4.9	5.5	1.9	11.7	5.2
b. Malignant neoplasm	3.0	2.9	2.8	6.5	2.9	1.1	6.1	2.4
c. Fracture	3.6	3.4	4.2	3.3	4.0	4.1	4.0	3.4
3 a Tonsillectomy	5.5	6.3	3.6	1.9	1.7	2.2	0.9	2.1
b. Appendectomy	2.4	2.6	2.1	1.4	1.3	1.4	1.0	1.1

Inpatients discharged with a primary diagnosis of malignant neoplastic disease were 3% of the total discharges from replying hospitals. The highest such percentage, 6.5, was for the discharges from state hospitals. As with cardiac disease, the percentage was also high, 6.1, for the Veterans Administration hospitals.

The 3,227 general and special hospitals that answered question 2c reported that 501,629 of the inpatients discharged in 1954 had a primary diagnosis of fracture. It is estimated that the corresponding number for the nonreplying hospitals was 219,662, thereby bringing to 721,291 the 1954 total for all general and special hospitals. This estimate was rounded to 720,000 on the chart. Patients with fractures were 3.6% of the discharges from all replying hospitals and 4.2% of the discharges from local governmental hospitals.

Size of Hospital.—Estimates made when the replies were grouped by size of hospital (see appendix tables) gave 979,374 as the total of cardiac cases—or only about 10,000 fewer than the estimate obtained for the type-of-control classification. The percentage (of total discharges) for the replying hospitals ranged from 4 for hospitals having 25 to 49 beds to 5.8 for hospitals having 500 or more beds. The estimated totals were 30,000 fewer for malignant neoplastic disease and 3,000 more for fractures when computations were based on size classifications of hospitals.

Hospital by Region.—When estimates were based on hospitals grouped according to their regional location, shown on appendix tables, the estimated totals for the nonreplying hospitals for cardiac disease and malignant neoplastic disease fell midway between the estimates based on type of control and bed size. The highest cardiac ratio was 5.5% for the Pacific region, and the lowest was 4.1% for the east south central and mountain regions. The malignant neoplastic disease ratio was highest, 3.4%, for the middle Atlantic region and lowest, 2.3%, for the mountain region. The ratios for fractures varied little from the average of 3.6%, with the possible exception of the Pacific region, where it was 3.9%.

Tonsillectomies and Appendectomies

Approximately 94% of the replying hospitals (slightly less than 4,100) answered question 3. There is no reason to believe that, for the general and special hospitals, the results would have been different had operations performed on "discharged inpatients" rather than on "inpatients" been requested. For the mental and tuberculosis hospitals, however, it may be that a few of the tonsillectomies and/or appendectomies were performed on persons who were still inpatients at the end of 1954. However, since the tonsillectomies and appendectomies reported by the mental and tuberculosis hospitals are only 0.1% and 0.2% of the total numbers of these operations (see appendix table), there is little reason for not continuing to use "discharged inpatients" as the base for the computation of ratios.

As shown in table 3, 813,139 tonsillectomies were performed on inpatients in 4,088 replying hospitals; 812,244 or 99.9% of these were in general and special hospitals, with only 895 in mental and tuberculosis hospitals. Our estimate of 288,326 such operations for the 2,882 nonreplying hospitals raises the total number to 1,101,465 (rounded to 1,100,000 on the chart). The ratios were 5.4% for all hospitals, 5.5% for general and special hospitals, and 0.3% for the mental and tuberculosis hospitals. Considering only the general and special hospitals (table 4), the highest ratio of tonsillectomies performed on inpatients was 6.3% for the nongovernmental hospitals; the lowest such ratio was 0.9% for the Veterans Administration hospitals. Indeed, for all of the seven breakdowns according to type of control the ratios were markedly different from the average ratio of 5.5%.

The same hospitals reported 358,148 appendectomies, only 0.2% (832) of which were performed in mental and tuberculosis hospitals. It is estimated that an additional 127,814 appendectomies were performed in the 2,882 nonreplying hospitals and that the total number of these operations in 6,970 hospitals accepted for listing in 1954 was 485,962 (raised and rounded to 500,000 on the chart). The ratios were 2.4% for all hospitals, 2.4% for general and special hospitals, and 0.3% for mental and tuberculosis hospitals (table 3). The appendectomy ratios for the seven different types of general and special hospitals ranged from 2.6% for the nongovernmental hospitals to 1% for the Veterans Administration hospitals. In state general and special hospitals the ratios for these two operations were, of course, much lower than the corresponding ratios for all hospitals—a sharp contrast to the higher ratio for malignant neoplastic disease. More than 80% of both of these operations were, however, performed in nongovernmental hospitals, with city and county controlled hospitals accounting for most of the remainders.

Size of Hospital.—Appendix tables reveal that about 30% of the tonsillectomies and appendectomies were performed in hospitals having 100 to 199 beds, while about 10% of these operations were performed in hospitals with 50 or fewer beds. The largest hospitals, those having 500 or more beds, discharged only about 6% and 8% of the tonsillectomy and appendectomy patients respectively. The smallest hospitals, those having fewer than 25 beds, discharged relatively more tonsillectomy (7.8%) and appendectomy (3.6%) patients out of their total discharges than any other class. More generally, these ratios were lower for hospitals with more beds—both for all hospitals and for general and special hospitals. In the mental and tuberculosis hospitals (see appendix tables), approximately three-fourths of these operations were performed in the largest hospitals, and it was only for the Veterans Administration mental and tuberculosis hospitals that the ratios approach 1%. When estimates were prepared for nonreplying hospitals according to seven size classifications, the total number of tonsillectomies was raised by only 34,000 and the number of appendectomies by only 18,000.

Hospitals by Region.—Since the east north central region had the greatest number of replying hospitals and the greatest number of admissions and discharges, it is consistent that the largest number of tonsillectomies and appendectomies was reported by this region (see appendix tables). The ratio of tonsillectomies to discharges was highest for New England (6.3%) and lowest for the east south central region (4.1%). The ratios of appendectomies to discharges varied little from the average of 2.4% of all regions (see appendix tables).

Summary

Of the discharged inpatients treated in hospitals by physicians in calendar year 1954, 18.4% were classified as obstetric. These totaled approximately 3,800,000—about 500,000 more than the number of births in hospitals reported by the A. H. A. for the 12-month period ending Sept. 30, 1954. Physicians performed one or more surgical procedures on 39.4%, or about 8,100,000, of their hospitalized patients in the calendar year 1954. Among these procedures were about 1,100,000 tonsillectomies and about 500,000 appendectomies. Hospitalized patients who had these two operations performed by their physicians were 5.4% and 2.4%, respectively, of the total inpatients discharged during the year. For the discharged patients from only nongovernmental general and special hospitals, these ratios were 6.3% for tonsillectomies and 2.6% for appendectomies.

In addition to the broad classifications of "obstetric inpatients discharged" and "inpatients discharged upon whom one or more surgical procedures were performed," there were about 8,800,000 "All other" inpatients discharged during the calendar year 1954. These included patients being treated in hospitals for a great variety of conditions; it also included some well persons who were briefly hospitalized by their physician for "physical check-ups" by the total medical care team.

With all types of general and special hospitals (from which 98.3% of all inpatients were discharged) considered, an estimated 4.9%—or about 1 million inpatients—had a primary diagnosis of some form of cardiac disease. About 585,000 of the total inpatients, discharged from these hospitals in 1954 had a primary diagnosis of some form of malignant neoplastic disease; this was 3% of the number discharged. About 720,000 of these discharged inpatients, or 3.6% of the total, were discharged with a primary diagnosis of fracture. These three diagnostic categories are mutually exclusive of one another, and they accounted for a total of 11.5% of all inpatients discharged from Veterans Administration hospitals. Malignant neoplastic disease accounted for 6.5% of the discharges from state hospitals and fractures for 4.2% of those from local governmental hospitals.

Since it is probable that most, if not all, of the fracture cases were also accident cases, one interesting result of this survey is that at least 22% of the patients treated by physicians in hospitals in 1954 and discharged therefrom did not have diseases but were hospitalized for conditions related to pregnancy (18.4%) or to accidents (3.6%). Moreover, because accidents can and do result in many more diagnostic conditions than "fractures," it is likely that the true percentage of patients treated in hospitals by physicians for conditions due to disease will be found to be less than 78%.

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MEDICAL NEWS

CALIFORNIA

Heart Association Moves.—The Los Angeles County Heart Association has moved to new headquarters at 660 S. Western Ave., Los Angeles 5, in the Franklin Life Building (telephone, DUnkirk 5-4231). This move effects a consolidation of the administrative and program offices, formerly located at 316 S. Bonnie Brae St., and the heart fund headquarters, formerly located at 5501 Wilshire Blvd.

New Orthopedic Hospital.—Plans have been approved for the construction of a $3,780,000 hospital to be built on the present site of the Orthopaedic Hospital at 24th and Flower streets in Los Angeles. The six-story structure, which will replace the 42-year-old main building, will provide 128 bed spaces, remodeled outpatient clinics, and four surgical rooms. The building will increase bed capacity by 50. The hospital will also enlarge its research and training program.

Dr. Kempe Goes to Colorado.—Dr. C. Henry Kempe, formerly assistant professor of pediatrics, University of California School of Medicine, San Francisco, has been named head of the department of pediatrics at the University of Colorado School of Medicine in Denver, succeeding Dr. Robert H. Alway, who resigned in 1955 to join Stanford University School of Medicine, Stanford University—San Francisco. Dr. Kempe was scheduled to arrive in Denver about Nov. 1. In 1955 Dr. Kempe was on leave to the Rockefeller Virus Laboratory in Rome on a Fulbright research grant. He has also carried out virus research in India and Indochina.

ILLINOIS

Chicago

Dr. Lawless Honored.—Kupat Holim, the medical department of the Israeli Federation of Labor, will establish a 35-bed T. K. Lawless Dermatology Department as a part of the Beilinson Hospital in Israel, an institution of 700 beds, where medical students of Jerusalem University take their clinical training. The dermatology department will cost $440,500, of which $160,500 will be raised in the United States by friends of Dr. Lawless of Chicago. Kupat Holim has constructed a system of 14 hospitals similar to those recently completed in the United States by the United Mine Workers. The new T. K. Lawless Dermatology Department will serve as a consultation and research center for all Kupat Holim institutions in Israel. Kupat Holim honored Dr. Lawless "in recognition of his stalwart accomplishments as a medical practitioner and teacher. In acknowledgement of his broad humanitarianism which transcends the boundaries of race and creed. In appreciation of his generous support of the State of Israel and its people."

KANSAS

Jordan Memorial Fund.—Friends of Dr. Ralph E. Jordan, Emporia, who died of bulbar poliomyelitis on July 10, have initiated a memorial fund to be used for the education of his six children. Anyone wishing to contribute may send a check to Mr. Ivan Anderson, Administrator, Newman Hospital, Emporia.

KENTUCKY

Personal.—The University of Louisville School of Medicine announces the appointment of Dr. Malcolm D. Thompson as professor of surgery and Dr. DeLou P. Hall as associate professor of surgery.——Dr. Robert D. Collins, currently on active duty at the Army Research Laboratory, Fort Knox, has been awarded a senior research fellowship by the U. S. Public Health Service. Following his release from the service, Dr. Collins will spend two years studying basic processes in the inflammatory reaction, after which he will return to the department of pathology, Vanderbilt University School of Medicine, Nashville, Tenn., as an assistant professor.

LOUISIANA

Tulane Promotions.—Tulane University School of Medicine, New Orleans, announces recent faculty promotions. Promoted to the rank of associate professor are Dr. Gustav C. Bahn, opthalmology; Dr. Joseph V. Hopkins, clinical medicine; Drs. Robert H. Lennox and Christopher H. Snyder, pediatrics; and Drs. John W. S. Hunt, William J. Mogabgab, John C. S. Paterson, and Walter G. Unglaub, medicine. Newly appointed assistant professors are Dr. Charles C. Abbott, surgery; Dr. Ralph W. Buddington Jr., clinical psychiatry; Dr. Cornelia A. Eddy, microbiology; Dr. David J. Farwell, otolaryngology; Dr. Henry M. Gelfand, epidemiology; Dr. Martin Goldfield, medicine; Drs. Francis M. Harris Jr., Stephen L. Madey, and Emma L. Sailors, pediatrics; Richard G. Hibbs, Ph.D., anatomy; Dr. Ruth D. Paterson, neurology and medicine; Dr. Neill K. Weaver, clinical medicine and public health; and Robert G. Yaeger, Ph.D., medicine and tropical medicine and public health.

Laboratory for Metabolic Research.—The Urban Maes Laboratory for endocrine and metabolic research was recently established in New Orleans under the auspices of the Urban Maes Research Foundation and the joint sponsorship of the Louisiana State University and Tulane University schools of medicine and Touro Infirmary, New Orleans. Temporary facilities will be established at the Louisiana State University School of Medicine until a permanent laboratory is constructed at Touro Infirmary. Dr. Floyd R. Skelton, former assistant professor of pathology at the Medical College of Georgia, Augusta, and now associate professor of pathology at Louisiana State University School of Medicine, is director of the laboratory. Funds to equip and operate the laboratory will come from public subscriptions, the research foundation, grants from federal agencies, and other sources. Dr. Hans Selye, director of the Institute of Experimental Medicine and Surgery, University of Montreal, Canada, was the principal speaker at the dedication ceremonies.

MASSACHUSETTS

Dr. Martha Eliot Goes to Harvard.—Dr. Martha M. Eliot, chief, U. S. Children's Bureau in Washington, D. C., has been appointed professor and head of the department of maternal and child health at Harvard University School of Public Health, Boston. On Jan. 1, 1957, she will succeed Dr. Harold C. Stuart, who helped to found the department in 1927 and who asks to be relieved of administrative duties and direction of the department's teaching program so that he may devote most of his time to research. Dr. Stuart will continue as a member of the department staff and will concentrate on the completion of a child growth and development study for which he and colleagues have been accumulating data since 1930. Dr. Eliot has directed the activities of the children's bureau in the U. S. Department of Health, Education, and Welfare since 1951. She is currently the U. S. representative on the board of the United Nations' International Children's Emergency Fund. She is a past-president of the American Public Health Association (1947-1948) and the National Conference of Social Work (1949).

Personal.—Dr. Hans Waine, Newton, has been appointed chief of staff of the Boston dispensary, a unit of the New England Medical Center, Boston. The office of chief of staff is a new medical appointment in the development and expansion program of the dispensary, which is constructing a million-dollar rehabilitation institute. Dr. Waine will work with Tufts College Medical School, Boston, and the other New England Medical Center units.——Dr. William A. McCausland, Norwell, has been appointed medical director of Hood Rubber Company, a division of the B. F. Goodrich Company, Watertown.——Dr. Laurence L. Robbins, chief, department of radiology, Massachusetts

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

General Hospital, Boston, was recently chosen the George Winslow Holmes Lecturer for 1956. His topic was "The Radiologist Faces Automation." After the lecture before the annual meeting of the New England Roentgen Ray Society, a silver Paul Revere pitcher was presented to him.—Dr. Joseph W. Gardella, research associate in medicine, Harvard Medical School, has been named assistant dean for student affairs in the faculty of medicine, Harvard University, succeeding Dr. William F. Ketchum, who plans to return to private practice. At Harvard College, Dr. Gardella was captain of the varsity football team in 1940.

MINNESOTA

Dr. Huenekens Honored.—Dr. Edgar J. Huenekens was honored for his long service to pediatrics and to the community at a recent banquet in Minneapolis, sponsored by members of the Minneapolis Pediatric Society, most of whom received their professional training under Dr. Huenekens. A library fund, bearing Dr. Huenekens' name, has been established for the future Children's Hospital in Minneapolis.

Gray Memorial Fund.—The Howard K. Gray Memorial Fund, in memory of Dr. Gray, head of a section of surgery at the Mayo Clinic from 1935 until his death, Sept. 6, 1955, will provide grants to fellows or former fellows of the Mayo Foundation for travel and other expenses incidental to visits to leading surgical centers in the United States and Canada. The recipients will be nominated by a committee consisting of the director of the Mayo Foundation, the chairman of the Surgical Society of the Mayo Clinic, all surgeons who serve as members of the board of governors of the Mayo Clinic, and such other persons as may be selected. Contributions thus far are sufficient to assure a return income that will allow the recipient to spend at least two weeks at some American surgical center.

Blood Bank Dedicated.—The $400,000 Minneapolis War Memorial Blood Bank was dedicated on Nov. 11 at 2303 Park Ave., South, with Dr. Leroy E. Burney, surgeon general, U. S. Public Health Service, Washington, D. C., as guest speaker. The bank will collect blood for the use of all hospitals in the community and will provide (1) a central depository where various groups can deposit their blood to their credit and have it available when needed at any point in the city; (2) a community-controlled reserve of plasma adequate for ordinary disasters; (3) a technical laboratory team to assist in transfusion problems, to study transfusion reactions, and to contribute to transfusion safety; and (4) a completely equipped laboratory in which to carry out studies of Rh and other hereditary antigens in blood. G. Albin Matson, Ph.D., is director of the bank.

MISSOURI

Personal.—Dr. Walter J. Burdette was recently appointed professor of clinical surgery at the St. Louis University School of Medicine, director of the St. Louis University surgical service at Veterans Hospital, and cancer coordinator for the school of medicine.

Hospital News.—The Jewish Sanatorium has moved from Fee Fee Road, Robertson, to new quarters at the Jewish Hospital medical center, 216 Kingshighway Blvd., St. Louis, where the sanatorium patients will be cared for in the 68-bed chronic disease division of the Mark C. Steinberg Memorial Hospital. The move is part of a larger project integrating the facilities and program at the sanatorium, the Miriam Rosa Bry Convalescent-Rehabilitation Hospital, Webster Groves, and the Jewish Medical Social Service Bureau into one large medical center at the Jewish Hospital of St. Louis.

NEW YORK

Premature Baby Care.—The New York State Department of Health has approved Samaritan Hospital in Troy as a center for premature baby care. Parents of premature infants born in Samaritan Hospital may receive financial assistance from the state and county if the extended care necessary for premature infants represents a financial problem. Parents of such premature infants may apply to the Rensselaer County Health Department for the financial assistance, which must be authorized by the Rensselaer County Children's Court.

Dr. Taylor's Centennial.—Dr. J. Richard Taylor, Brooklyn, descendant of President Zachary Taylor, celebrated his 100th birthday, Nov. 22. Dr. Taylor served in the Spanish-American War, was surgeon in charge of the Johnstown Flood emergency operation, and was influential in the opening of the Northwest Territory. Now a resident of the Buckminster Nursing Home, 630 Ocean Ave., he is said to be the oldest living graduate of the University of Pennsylvania School of Medicine, Philadelphia.

Faculty Promotions.—The State University of New York College of Medicine in Syracuse announces the following promotions:

Department of radiology: Dr. Paul A. Riemenschneider, full professor; Dr. Alfred S. Berne, associate professor; and Dr. Alfred Schick, assistant professor.

Department of surgery: Dr. Lloyd S. Rogers, associate professor; and Drs. William L. Parry, George A. Sisson, Bernard S. Piskor, Donald F. Buschle, Paul M. Cramer, Jacob S. Israel, Clifford J. Straehley Jr., and Frederick E. Wetherell, clinical assistant professors.

Department of medicine: Drs. Max Kutzer and Paul C. Clark, clinical professors; Drs. Robert E. Westlake and William A. Schiess, clinical associate professors; and Drs. George R. Burnett, Benjamin F. Levy, Murray A. Grossman, Irving Swartz, and Armand U. Aquilino, clinical assistant professors.

Department of otolaryngology: Drs. David W. Brewer, Lee R. Stoner Jr., and Richard L. Sullivan, clinical associate professors; Drs. David L. Poushter and Wesley H. Bradley, clinical assistant professors; and Dr. George G. Lerner, assistant professor.

Department of obstetrics: Dr. Albert W. Van Ness, clinical professor; and Dr. James N. Capps, clinical assistant professor.

New York City

Lecture on Neoplastic Diseases.—In its series of lectures on neoplastic diseases, Montefiore Hospital will offer "Carcinoma of the Ovary" by Dr. Howard C. Taylor Jr., professor of obstetrics and gynecology, Columbia University College of Physicians and Surgeons, Jan. 4, 1957, at 3 p. m., in the West Basement Conference Hall.

New Psychiatry Professor at Social Work School.—Dr. Maurice R. Friend, lecturer at the State University College of Medicine Psychoanalytic Institute, has been appointed the first professor of psychiatry to occupy the recently established Marion E. Kenworthy Chair in Psychiatry at the New York School of Social Work, Columbia University. The chair was created by a $400,000 endowment fund contributed by friends of Dr. Marion E. Kenworthy on her retirement as professor of psychiatry at the school. Dr. Friend will continue in private practice.

TENNESSEE

Personal.—Dr. Virgil S. LeQuire, assistant professor of anatomy, Vanderbilt University School of Medicine, Nashville, has been awarded a senior research fellowship by the U. S. Public Health Service. The title of his project is "Vascular Embolization."

WEST VIRGINIA

Camp for Handicapped Children.—According to the West Virginia State Medical Association, Galahad, the new camp for handicapped children, now under construction at Quick, 35 mi. northeast of Charleston, will be used next summer by diabetic and blind children of the state. A continuing statewide fund-raising campaign is in progress. Dr. Richard V. Lynch Jr., Clarksburg, and Drs. John H. Gile and Oliver H. Brundage, Parkersburg, are members of the planning committee.

Personal.—Dr. William S. Herold, Fayetteville, has been appointed health officer of Fayette County.—Dr. Guy R. Post, Parkersburg, director of the Wood County-Parkersburg Health Department, has been named a member of the Royal Society of Health of London.—Dr. Laurence L. Duncan, a native of Charleston, has been named assistant professor of pathology at West Virginia University School of Medicine, Morgantown. He interned at Henry Ford Hospital in Detroit and recently completed a residency in surgery at the Veterans Administration Hospital in Houston, Texas.—Dr. Helen B. Fraser, Charleston, director, division of maternal and child health, state department of health, since 1952, recently resigned to accept appointment as director, division of maternal and child health, Kentucky State Department of Health, with headquarters in Louisville.—Lieut. E. Lowell Berry, M. C., U. S. Naval Reserve, who has been on duty at the Boston Naval Shipyard dispensary for two years, has accepted appointment in Pittsburgh as chief, division of industrial health, Allegheny County Department of Health, and as lecturer in occupational medicine, University of Pittsburgh Graduate School of Public Health.

GENERAL

Seminar in Plastic and Reconstructive Surgery.—The American Otorhinologic Society for Plastic Surgery will hold a seminar in plastic and reconstructive surgery of the head and neck at the Louisiana State University School of Medicine, New Orleans, Feb. 17-23, 1957. Information may be obtained from Dr. Louis J. Feit, Secretary, 66 Park Ave., New York 16.

Award in Proctology.—The International Academy of Proctology announces its annual award contest for 1956-1957 in which the best unpublished contribution on proctology or allied subjects will be awarded $100 and a certificate of merit. Entries (limited to 5,000 words, typewritten in English, and submitted in five copies) should be submitted before Feb. 1, 1957, to the International Academy of Proctology, 147-41 Sanford Ave., Flushing, N. Y.

Oscar Hunter Memorial Award.—The American Therapeutic Society invites nominations for the Oscar Hunter Memorial award, presented annually in honor of its late secretary, Dr. Oscar B. Hunter. The award consists of a bronze medal struck in the likeness of Dr. Hunter and engraved with the name of the recipient. The winner is expected to present a paper at the time of the award. Travel expenses to the meeting will be furnished. Nominations for the 1957 award should be submitted before Feb. 1 to Dr. Harry E. Ungerleider, 393 Seventh Ave., New York 1.

Kraepelin Commemorative Meeting.—During the 123rd annual meeting of the American Association for the Advancement of Science, Dec. 26-31, in New York City, a symposium, "Epidemiology of Mental Disorders," will be presented under the co-sponsorship of the American Psychiatric Association and the American Public Health Association at the Sky Top, Hotel Statler. The program, which will commemorate the centennial of the birth of Emil Kraepelin, has been arranged by Dr. Benjamin Pasamanick, Ohio State University Health Center, Columbus. It will open at 9 a. m. Thursday with the memorial lecture by Dr. Eugen Kahn, Houston, Texas. In all, 12 presentations will be made.

Program of Engineering Section.—At the meeting of the American Association for the Advancement of Science, Statler Hotel, New York City, Dec. 26-27, the engineering section will present a program on "Aids for Environmental Control," which will open Wednesday, 9:30 a. m., with "Overcoming Normal and Abnormal Physical Limitations." Wednesday afternoon the session on "Extending Mental and Rational Powers" will be opened by Dr. Charles M. Gratz, New York City, whose subject will be "Biomechanics in Crash Mortality: The Surgical Approach Coordinating Man's Built-in Crash Defenses." The Thursday morning program will consist of four papers: "Translating Teletypesetter Tape to Braille," "Reduction of Speech Signals for Easier Transmission," "Mechanical Translation of German," and "Mechanical Translation of Russian."

Millions in Grants for Cancer Research.—The American Cancer Society, which recently reorganized its research program, announces that it can distribute at least 7 million dollars in 1957 to individual scientists and research institutions prepared to investigate problems pertinent to cancer control. Application forms may be obtained by writing to the American Cancer Society, 521 W. 57th St., New York 19. Applications received before Jan. 1 will be acted on during the late winter and early spring, and most grants will become effective July 1, 1957. Other deadlines for receipt of applications will be May 1 and Sept. 1. Types of grants include project grants, program grants, institutional research grants, contracts for research, postdoctoral fellowships, scholarships in cancer research, and additional faculty-level positions.

Course on Diseases of the Chest.—The sixth biennial postgraduate course on diseases of the chest, co-sponsored by the Los Angeles County Tuberculosis and Health Association and the Los Angeles County Medical Association, will be given Jan. 31–Feb. 2 in Los Angeles. Among many other things on the program will be a cancer workshop, with division of the class into small groups involving a panel composed of a surgeon, an internist, and a pathologist. An optional feature on Wednesday will be specially arranged observations of local hospital clinics, activities, and conferences. The faculty will include Drs. David T. Carr, Rochester, Minn.; Maurice S. Segal, Boston; Edgar W. Davis, Washington, D. C.; H. Corwin Hinshaw, San Francisco; and local chest specialists. The registration fee of $35 will include a banquet on Thursday evening. Information may be obtained by writing to Dr. David Salkin, 1670 Beverly Blvd., Los Angeles 26.

Fourth Fatal Case of Rabies.—According to the U. S. Public Health Service, S. Edward Sulkin, Ph.D., Southwestern Medical School of the University of Texas, Dallas, has reported a fatal case of human rabies, the fourth in the area during the current year. The victim was a 63-year-old man whose death followed an incubation period of 54 days. The California State Department of Public Health has reported a total of 264 cases of rabies in animals for the period Jan. 1–Oct. 9, 1956. Of these, 126 were in dogs, 101 in skunks, and 27 in cattle. The remainder were in various domestic and wild animals. Dr. Walton H. Y. Smith, Montgomery, Alabama State Department of Public Health, has reported the second case of bat rabies within one month. A bat with symptoms of rabies captured in Mobile County showed Negri bodies in its brain tissue. Rabies virus was isolated from both the brain and salivary glands at the Virus and Rickettsia Laboratory, U.S. Public Health Service, Montgomery. The bat was identified as an insectivorous species, *Lasiurus borealis borealis*.

Grant for Mental Health Study.—Dr. Jack R. Ewalt, director of the three-year national mental health study recently initiated by the Joint Commission on Mental Illness and Health (808 Memorial Dr., Cambridge, Mass.) has announced receipt of $25,000 from the Smith, Kline and French Foundation of Philadelphia for support of the commission's work. The purposes of the commission's study are to appraise mental health knowledge and methods and find new approaches to combating mental illness or better ways of implementing existing methods. The study was undertaken under a 1955 Act of Congress authorizing the National Institute of Mental Health to grant $1,250,000 and providing for acceptance by the commission of additional support from nongovernmental sources. The Smith, Kline and French grant is the first received from private foundations or industrial sources as a supplement to the government funds. Dr. Kenneth E. Appel of Philadelphia is president of the Joint Commission on Mental Illness and Health and Dr. Leo H. Bartemeier of Baltimore is chairman of its board of trustees.

Continental Casualty Research Grants.—The Continental Casualty Company has established grants in support of promising research in student medicine to encourage investigation that will promote the health of college students and benefit student medical practices. Two grants of $500 will be made annually, one to support research in a college of less than 2,000 enrollment, the other in a college of more than 2,000 enrollment. Grants can be used for either clinical or experimental research (1) as the sole source of support for exploratory or small-scale studies or (2) in conjunction with college or other funds to support sections of a large-scale research project. Grant recipients will be selected by the committee on research of the American College Health Association. Member colleges are invited to submit research proposals (six copies) at any time. Recipients, to be announced at the annual meeting of the association, will be based on all proposals received by Feb. 1 of that year. Proposals may be mailed to John Summerskill, Ph.D., Chairman, Committee on Research, Student Medical Clinic, Cornell University, Ithaca, N. Y.

Research Centers in Higher Education.—The Carnegie Corporation of New York, 589 Fifth Ave., New York 17, has issued a list of grants totaling almost 2 million dollars and providing for

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DEATHS

Lyman, David Russell ⊕ Wallingford, Conn.; born in Buffalo, N. Y., March 8, 1876; University of Virginia Department of Medicine, Charlottesville, 1899; past-president of the New Haven County Medical Society, Connecticut State Medical Society, American Sanatorium Association, Connecticut Tuberculosis Association, and American Climatological and Clinical Association; a founder and past-president of the National Tuberculosis Association, which in 1943 awarded him the Trudeau medal; member of the American Trudeau Society; during World War I served with the American Red Cross in France and was a member of the commission for the prevention of tuberculosis in France; an associate fellow of Branford College of Yale University, New Haven; a member of the council of the Henry Phipps Institute of the University of Pennsylvania in Philadelphia; held honorary degrees from Yale University, New Haven, and Wesleyan University, Middletown; a director of the First National Bank; for many years superintendent of the Gaylord Farm Sanatorium, where since 1953 was superintendent emeritus; died in the Grace-New Haven Community Hospital, New Haven, Oct. 15, aged 80, of leukemia.

Aubrey, John Forsyth, Miami, Fla.; born in Lynchburg, Va., Nov. 25, 1883; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1921; an associate member of the American Medical Association; member of the Medical and Chirurgical Faculty of Maryland; for many years practiced in Baltimore, where he was physician on the board of education; for 17 years surgeon of the Maryland State Penitentiary in Baltimore; medical officer with the 29th division, National Guard, during World War II and served as depot surgeon of the Philadelphia Signal Depot; retired as a colonel in 1946 after 23 years in the Army Reserve; veteran of World War I; died in the Mount Alto Veterans Administration Hospital, Washington, D. C., Oct. 4, aged 72, of paralysis agitans and cerebral atrophy.

Stephens, Philip Howard, Chino, Calif.; Washington University School of Medicine, St. Louis, 1899; formerly on the faculty of the College of Medical Evangelists, Loma Linda and Los Angeles; an associate member of the American Medical Association; member of the American Association for the Surgery of Trauma and the Industrial Medical Association; fellow of the American College of Surgeons; past-president of the Los Angeles County Medical Society; on the staffs of the Hospital of the Good Samaritan, Presbyterian Hospital-Olmsted Memorial, and the Cedars of Lebanon Hospital in Los Angeles; served as chief surgeon of the Union Pacific Railroad and medical director of the Southern California Bell Telephone Company; died in the Hospital of the Good Samaritan, Los Angeles, Sept. 8, aged 80.

Boyes, Truman Leo ⊕ New York City; born in Mount Hope, Ontario, Canada, 1898; University of Toronto Faculty of Medicine, Toronto, Canada, 1922; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology and the Association for Research in Ophthalmology; fellow of the American College of Surgeons; clinical professor of ophthalmology at the New York University Post-Graduate Medical School; formerly on the faculty of the New York University-Bellevue Medical Center; on the staffs of the St. Mary's Hospital in Hoboken, N. J., New York Eye and Ear Infirmary, Misericordia Hospital, and the Manhattan Eye, Ear and Throat Hospital; died in the Doctors Hospital Oct. 17, aged 58, of a heart attack.

McCamant, Thomas Jefferson ⊕ El Paso, Texas; Fort Worth School of Medicine, Medical Department of Fort Worth University, Fort Worth, 1902; past-president of the El Paso County Medical Society; served as president of the Texas Public Health Association; veteran of the Spanish-American War and World War I; during World War II served as chairman of procurement and assignment of physicians for the Armed Forces; formerly city and county health officer; in 1935 a three county health unit, comprising El Paso, Hudspeth, and Culbertson counties, was established under his supervision; on the staffs of the Southwestern General Hospital and the Hotel Dieu, Sisters' Hospital; died Sept. 2, aged 82, of coronary occlusion.

Gervin, Peter Alphonse, San Diego, Calif.; born in Athol, Mass., Aug. 20, 1920; Tufts College Medical School, Boston, 1946; certified by the National Board of Medical Examiners; interned at the U. S. Naval Hospital in Corona; formerly a resident at the City Memorial Hospital in Winston-Salem, N. C., and the San Diego County General Hospital; served in the U. S. Naval Reserve; on the staffs of the Mercy Hospital, Balboa Hospital, Quintard Hospital, Villa View General Hospital, La Mesa (Calif.) Community Hospital, and the Chula Vista (Calif.) Hospital; died Sept. 24, aged 36, of sarcoma.

Gibson, Stanley ⊕ Chicago; born April 9, 1883; Northwestern University Medical School, Chicago, 1913; specialist certified by the American Board of Pediatrics; professor of pediatrics emeritus at his alma mater; member of the American Pediatric Society, Institute of Medicine of Chicago, and the American Academy of Pediatrics; veteran of World War I; served on the staffs of St. Luke's Hospital and the Children's Memorial Hospital; in 1949 DePauw University, Greencastle, Ind., awarded him an honorary doctor of science degree; died in the Veterans Administration Research Hospital Oct. 24, aged 73, of cancer.

Alexander, John Eugene, Charlotte, N. C.; Meharry Medical College, Nashville, Tenn., 1930; consultant, Good Samaritan Hospital; died Sept. 25, aged 53.

Allen, Wilmot B., New York City; Baltimore Medical College, Baltimore, 1898; member of the Medical Society of the State of New York; consulting ophthalmologic surgeon at St. Francis' Hospital; one of the founders of the Bronx Eye and Ear Infirmary, where he was consultant in ophthalmology and for many years secretary of its board of trustees; honorary assistant eye surgeon at New York Eye and Ear Infirmary; died in St. Luke's Hospital Oct. 12, aged 81, of ruptured abdominal aortic aneurysm.

Aydelotte, Benjamin Fisher ⊕ Louisville, Ky.; University of Louisville School of Medicine, Louisville, 1933; member of the Southeastern Surgical Congress; fellow of the International College of Surgeons; veteran of World War II; for many years on the staffs of the St. Joseph Infirmary and Kentucky Baptist Hospital; died Sept. 30, aged 57, of cancer.

Bate, Richard Alexander, Louisville, Ky.; Hospital College of Medicine, Louisville, 1892; formerly on the faculty of his alma mater; served on the staffs of St. Joseph and Norton Memorial infirmaries and SS. Mary and Elizabeth, Kentucky Baptist, and Jewish hospitals; died Oct. 6, aged 85, of uremia and cerebral arteriosclerosis.

Beil, John Wallace ⊕ Kansas City, Mo.; University Medical College of Kansas City, 1901; member of the American Academy of Ophthalmology and Otolaryngology; specialist certified by the American Board of Ophthalmology; veteran of the Spanish-American War; on the staff of St. Joseph Hospital; died Sept. 22, aged 81, of arteriosclerosis.

Biggar, Robert John ⊕ Awali, Bahrein Islands in Persian Gulf; Wayne University College of Medicine, Detroit, 1937; veteran of World War II; medical director of the California-Texas Oil Company; died Sept. 21, aged 47.

Blender, William ⊕ Peoria, Ill.; Keokuk Medical College, College of Physicians and Surgeons, Keokuk, Iowa, 1904; past-president of the Peoria Medical Society; member and past-president of the staff, St. Francis Hospital, where he died Sept. 27, aged 73.

Borodkin, Howard David, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1953; certified by the

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⊕ Indicates Member of the American Medical Association.

National Board of Medical Examiners; resident at the Hahnemann Medical College and Hospital, where he died Oct. 12, aged 31, of carcinoma of the colon.

Boyce, Addisone Schipper, New City, N. Y.; New York Medical College and Hospital for Women, Homeopathic, New York City, 1906; formerly on the faculty of her alma mater; served on the staffs of the Woman's Hospital and the Flower and Fifth Avenue Hospitals in New York City; died in the Doctors Hospital, New York City, Oct. 17, aged 73, of coronary thrombosis.

Brand, Andrew J. ⊕ Prairie, Miss.; Memphis Hospital Medical College, Memphis, Tenn., 1901; died Oct. 6, aged 86.

Brown, James Adlai, Jr. ⊕ Evansville, Ind.; Howard University College of Medicine, Washington, D. C., 1934; veteran of World War II; on the staffs of the Protestant Deaconess Hospital and St. Mary's Hospital, where he died Sept. 25, aged 50, of pancreatitis and hepatitis.

Burhyte, Egbert L. ⊕ Niagara Falls, N. Y.; University of Buffalo School of Medicine, Buffalo, 1911; member of the Industrial Medical Association; fellow of the American College of Surgeons; on the staffs of the Mount St. Mary's Hospital and the Niagara Falls Memorial Hospital, where he was chief of staff and chief of surgery and where he died Sept. 27, aged 70, of cerebral thrombosis.

Carliner, Paul Elliott ⊕ Baltimore; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1934; also a graduate in pharmacy; member of the American Academy of Allergy; veteran of World War II; instructor in medicine at Johns Hopkins University School of Medicine; on the staffs of the Sinai Hospital and the Johns Hopkins Hospital, where he died Oct. 13, aged 46, of a heart attack.

Clayton, Ione Shultz ⊕ Arkansas City, Kan.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, Chicago, 1908; died Sept. 16, aged 71, of cerebral hemorrhage.

Collins, Edward Ladow, Grand Rapids, Mich.; Detroit College of Medicine and Surgery, Detroit, 1916; served as superintendent of the Michigan Employment Institute for the Blind in Saginaw; died Sept. 25, aged 77, of cerebral embolism, coronary occlusion, and arteriosclerosis.

Corby, John Francis ⊕ Colonel, U. S. Army, retired, Sonoma, Calif.; Medico-Chirurgical College of Philadelphia, 1913; served in France during World War I; veteran of World War II; entered the Medical Corps of the U. S. Army in 1917 and retired Sept. 30, 1946; died in the Letterman Army Hospital, San Francisco, Oct. 5, aged 64.

Croft, Marion Eugene, Hopkinsville, Ky.; University of Nashville Medical Department, Nashville, Tenn., 1900; Hospital College of Medicine, Louisville, 1902; honorary staff member of the Jennie Stuart Memorial Hospital, where he died Sept. 13, aged 81, of cerebral arteriosclerosis.

Crook, Roy, Downey, Calif.; John A. Creighton Medical College, Omaha, 1905; for many years practiced in Lincoln, Neb.; died Sept. 24, aged 76.

Cross, Earl William, Tarentum, Pa.; College of Physicians and Surgeons, Baltimore, 1908; an associate member of the American Medical Association; fellow of the American College of Surgeons; served on the staff of the Allegheny Valley Hospital; died in the Medical College of Virginia, Hospital Division, in Richmond Sept. 26, aged 69.

Deichler, Lyn Waller, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1903; an associate member of the American Medical Association; member of the American Academy of Ophthalmology and Otolaryngology; specialist certified by the American Board of Ophthalmology; consulting ophthalmologist at the Philadelphia General Hospital; died Oct. 2, aged 74, of coronary thrombosis.

Dietsche, Erwin Karl ⊕ Klamath Falls, Ore.; Albert-Ludwigs-Universität Medizinische Fakultät, Freiburg, Baden, Germany, 1910; died Sept. 30, aged 70, of coronary infarction.

Drake, Charles Arthur, Ridgewood, N. J.; Syracuse University College of Medicine, Syracuse, N. Y., 1908; formerly practiced in New York City, where he was on the staff of the New York Eye and Ear Infirmary; died Sept. 19, aged 72, of a heart attack.

Douglass, Charles William ⊕ Anacortes, Wash.; Creighton University School of Medicine, Omaha, 1941; member of the American Academy of General Practice; interned at the Providence Hospital in Seattle; past-president of the Skagit County Medical Association; served as city health officer; veteran of World War II; on the staff of the Anacortes Hospital; died Sept. 10, aged 41, of coronary occlusion.

Elfeld, Edward A., Arlington Heights, Ill.; Homeopathic Medical College of Missouri, St. Louis, 1891; died in St. Anthony Hospital, Denver, Oct. 5, aged 88, of arteriosclerotic heart disease.

Escue, Henry Merritt, Charleston, W. Va.; Medical College of Virginia, Richmond, 1932; specialist certified by the American Board of Urology; an associate member of the American Medical Association; member of the American Urological Association; fellow of the American College of Surgeons; veteran of World War II; served as mayor of St. Albans; past-president of the Kanawha Medical Society; died in the Charleston General Hospital Oct. 17, aged 53, of astrocytoma.

Ferris, John Charles ⊕ Senior Surgeon, U. S. Public Health Service Reserve, Texarkana, Texas; Laval University Faculty of Medicine, Quebec, Canada, 1940; chief medical officer for the Federal Correctional Institute; died in Long Beach, Calif., Sept. 21, aged 44, of cerebral hemorrhage and hypertension.

Floyd, Thomas J., Abbeville, Ala.; Medical Department of Tulane University of Louisiana, New Orleans, 1907; member of the Medical Association of the State of Alabama; served as city commissioner and Henry County health commissioner; formerly health officer of Houston County; died Sept. 25, aged 72, of coronary disease.

Foley, Edward Paul, Miami, Fla., Albany Medical College, Albany, N. Y., 1899; died Sept. 2, aged 82, of arteriosclerosis.

Ford, Ada, Mansfield, Ohio; University of Wooster Medical Department, Cleveland, 1909; died Sept. 28, aged 80.

Fort, Richard George ⊕ Glenview, Ill.; University of Illinois College of Medicine, Chicago, 1939; member of the American Academy of General Practice; veteran of World War II and was awarded the Bronze Star; on the staff of St. Francis Hospital in Evanston; died Oct. 2, aged 41, of acute myocardial infarction and arteriosclerotic heart disease.

Frank, John Henry, Neillsville, Wis.; Wisconsin College of Physicians and Surgeons, Milwaukee, 1896; died Aug. 29, aged 86, of coronary occlusion.

Gates, Benjamin Franklin ⊕ Cleveland, Tenn.; Medical Department of Grant University, Chattanooga, 1898; died Sept. 28, aged 94.

Gelow, John E., Grand Island, Neb., Northwestern University Medical School, Chicago, 1905; died in St. Joseph's Hospital, Brainerd, Minn., Sept. 22, aged 76.

Gibner, George P., Spearman, Texas; University of Texas School of Medicine, Galveston, 1897; died in the Hansford County Hospital Sept. 28, aged 83.

Gibson, Charles Francis, Burlington, N. J.; Howard University College of Medicine, Washington, D. C., 1931; formerly practiced in Mobile, Ala., where he was psychiatrist for the Veterans Administration and on the staff of the Blessed Martin de Porres Hospital; served on the board of health; died in the Deborah Tuberculosis Sanatorium, Browns Mills, Sept. 5, aged 50, of heart disease.

Glafke, William Harley ⊕ New York City; Northwestern University Medical School, Chicago, 1911; interned at the Cook County Hospital in Chicago; specialist certified by the American Board of Internal Medicine; consulting gastroenterologist at the Woman's Hospital; consulting physician in gastroenterology at St. Luke's Hospital, where he died Oct. 1, aged 70, of coronary thrombosis.

Gouldin, John Milton ⊕ Tappahannock, Va.; Medical College of Virginia, Richmond, 1904; past-president of the Mid-Tidewater Medical Society; died Sept. 10, aged 77.

Gray, Albert Newton ⊕ Burlington, Kan.; University of Kansas School of Medicine, Kansas City, 1907; served as county health officer and county coroner; on the staff of the Coffey County Hospital, where he died Sept. 20, aged 86, of cardiorenal vascular disease.

Gray, Henry Arthur ⊕ Keokuk, Iowa; College of Physicians and Surgeons, Keokuk, 1895; Keokuk Medical College, College of Physicians and Surgeons, Keokuk, 1900; fellow of the American College of Surgeons; past-president of the Iowa State Medical Society; veteran of World War I; for many years on the staffs of Graham Hospital and St. Joseph's Hospital, where he died Sept. 23, aged 83.

Guenther, Leo Peter ⊕ Los Angeles; Western Reserve University School of Medicine, Cleveland, 1923; member of the American Academy of General Practice; on the staff of the California Hospital, where he died Aug. 22, aged 58, of uremia.

Hallarman, Harry, New York City; University and Bellevue Hospital Medical College, New York City, 1913; died Oct. 9, aged 73, of coronary occlusion.

Havey, Leroy Austin, Bridgeport, Conn.; University of Vermont College of Medicine, Burlington, 1910; member of the Connecticut State Medical Society; served as treasurer of the Fairfield County Medical Association; died Sept. 28, aged 71, of acute myocardial infarction.

Hartzell, Solomon Mayer, Beverly Hills, Calif.; University of Pennsylvania Department of Medicine, Philadelphia, 1901; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the International College of Surgeons and the American College of Surgeons; formerly practiced in Youngstown, Ohio, where he was on the staff of the Youngstown Hospital; died in the Cedars of Lebanon Hospital, Los Angeles, Sept. 10, aged 76, of heart disease.

Heath, J. Mott, Greenport, N. Y.; College of Physicians and Surgeons, Baltimore, 1913; member of the Medical Society of the State of New York; examining physician for Greenport public schools; for many years president of the board of trustees and chief of staff of Eastern Long Island Hospital in Greenport; county coroner; died Sept. 20, aged 78, of arteriosclerosis.

Heim, John W. ⊕ Louisville, Ky.; Louisville Medical College, Louisville, 1904; member of the American Society of Anesthesiologists; served on the staffs of the SS. Mary and Elizabeth Hospital, St. Anthony Hospital, Jewish Hospital, Childrens Hospital, and the Kentucky Baptist Hospital, where he died Sept. 25, aged 75, of bronchogenic carcinoma, duodenal ulcer, and cholelithiasis.

Hinrichs, August Gustav, West Pittston, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1900, an associate member of the American Medical Association; served overseas during World War I; member of the staff of the Pittston Hospital, where he died Sept. 1, aged 80.

Hoffman, J. Omer ⊕ Chester, Ill., University of Arkansas School of Medicine, Little Rock, Ark., 1934; member of the American Academy of General Practice; past-president of the Randolph County Medical Society; vice-president of the medical staff of St. Clement's Hospital in Red Bud; veteran of World War II; died Sept. 4, aged 49, of coronary thrombosis.

Holt-Harris, John Evan, Albany, N. Y.; Albany Medical College, Albany, 1929; served as professor of bacteriology at his alma mater; formerly city bacteriologist; formerly on the staffs of the Willard Parker Hospital in New York City and the Albany Hospital, where he died Oct. 14, aged 79, of carcinoma of the sigmoid.

Hunt, Donald Jay ⊕ Senior Surgeon, U. S. Public Health Service, retired, Los Angeles; Northwestern University Medical School, Chicago, 1927; retired from the U. S. Public Health Service June 1, 1952; died Sept. 17, aged 56, of myocardial infarction.

Jameson, William Beatty, Bethlehem, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1886; served on the staff of the Hamburg State Sanatorium for Tuberculosis No. 3 in Hamburg; died Sept. 8, aged 96, of pulmonary edema.

Jenkins, George Bain, Washington, D. C.; Hospital College of Medicine, Louisville, Ky., 1898; professor emeritus of anatomy at the George Washington University School of Medicine; died Oct. 6, aged 81, of a heart attack.

Jennings, Cyrus Packard, Macedon, N. Y.; University of Buffalo School of Medicine, Buffalo, 1894; an associate member of the American Medical Association; died in the Park Avenue Hospital in Rochester, Aug. 22, aged 83, of arteriosclerosis.

Josey, Thomas Walter, Augusta, Ga.; Howard University College of Medicine, Washington, D. C., 1912; member of the board of directors of the Pilgrim Health and Life Insurance Company; died in Washington, D. C., Aug. 31, aged 75.

Kennedy, Edwin Jay, Houston, Texas; University of Texas School of Medicine, Galveston, 1918; retired chief medical examiner for the Army recruiting station; veteran of World War I; died Oct. 2, aged 64, of coronary thrombosis.

King, Luther John ⊕ Meadville, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1922; formerly secretary of the Crawford County Medical Society; formerly practiced in Conneautville, where he was a member of the school board; past-president of the Pennsylvania Allergy Association; for many years county coroner; on the staff of the Spencer Hospital; died Aug. 29, aged 59, of coronary thrombosis.

Krampert, Frank Lawrence ⊕ Auburn, Neb.; University of Nebraska College of Medicine, Omaha, 1921; died in the Auburn Hospital Aug. 24, aged 62, of cerebral hemorrhage.

Kuttler, Leonard William, Cleveland; Ohio State University College of Homeopathic Medicine, Columbus, 1915; died in the Euclid-Glenville Hospital Oct. 2, aged 72, of cerebral thrombosis.

Lapp, John G. ⊕ Kansas City, Mo.; University Medical College of Kansas City, 1897; formerly member of the city council; on the staffs of the Research Hospital and the Menorah Hospital Medical Center, where he died Sept. 23, aged 86, of prostatic hypertrophy.

Lawrence, Henry Dolson ⊕ Marietta, Pa.; Temple University School of Medicine, Philadelphia, 1930; Marietta school examiner; on the staff of the Columbia (Pa.) Hospital; died in the Lancaster (Pa.) General Hospital Oct. 1, aged 54.

Leonard, Frederick Jerome, Ilion, N. Y.; Syracuse University College of Medicine, Syracuse, 1911; an associate member of the American Medical Association; veteran of World War I; on the staff of the Ilion Hospital; died Sept. 22, aged 70, of cancer.

Levi, Max, New York City; Ludwig-Maximilians-Universität Medizinische Fakultät, München, Bavaria, Germany, 1923; member of the International College of Surgeons; on the staffs of the Mount Sinai Hospital and the Kew Gardens (N. Y.) General Hospital; died Oct. 9, aged 61, of a heart attack.

McKnight, William Burney ⊕ Mansfield, Texas; University of Louisville Medical Department, Louisville, Ky., 1886; died Oct. 1, aged 97.

Manny, Mary Alice ⊕ Laguna Beach, Calif.; Woman's Medical College of Pennsylvania, Philadelphia, 1927; on the staff of the Hoag Memorial Hospital–Presbyterian, Newport Beach; died Oct. 4, aged 63, of cancer of the throat.

Marlowe, William Anderson, Walstonburg, N. C.; Jefferson Medical College of Philadelphia, 1919; member of the Medical Society of the State of North Carolina; served as president of the Greene County Medical Society; veteran of World War I; died in the Woodard-Herring Hospital, Wilson, Sept. 29, aged 65, of heart disease.

Martin, James Calvin, Pulaski, Va.; University of Virginia Department of Medicine, Charlottesville, 1934; veteran of World War II; member of the Medical Society of Virginia; on the staff of the Pulaski Hospital; died Aug. 12, aged 48, of myocardial infarction.

Mason, Lyman Whidbee ⊕ Denver; University of Colorado School of Medicine, Denver, 1925; specialist certified by the American Board of Obstetrics and Gynecology; member of the Central Association of Obstetricians and Gynecologists; formerly on the faculty of his alma mater; member of the staffs of St. Joseph's Hospital and the Presbyterian Hospital; served as acting scientific editor of the *Rocky Mountain Medical Journal*; died Aug. 29, aged 60.

Massenburg, George Yellott ⊕ Macon, Ga.; University of Maryland School of Medicine, Baltimore, 1911; fellow of the American College of Surgeons; veteran of World War I; consultant, Macon Hospital; died in St. Mary's Hospital, Rochester, Minn., Sept. 1, aged 68, of embolus to coronary artery with heart failure and acute bacterial endocarditis.

Mauboules, Jean Paul, Jr., Rayne, La. (licensed in Louisiana in 1899); past-president of Rayne State Bank; died Sept. 30, aged 87.

Pan, Oscar ⊕ Cleveland; Deutsche Universität Medizinische Fakultät, Prague, Austria, 1902; served on the staff of St. Alexis Hospital; died Sept. 5, aged 79, of cardiovascular renal disease.

Parkerson, Isaac Jefferson, Eastman, Ga.; University of Georgia Medical Department, Augusta, 1917; veteran of World War I; died in the Veterans Administration Hospital, Dublin, Aug. 30, aged 67, of arteriosclerosis.

Porter, Arthur Silas ⊕ Salem, Ill.; Loyola University School of Medicine, Chicago, 1916; died Aug. 25, aged 81.

Price, Chester Arthur ⊕ Chicago; Eclectic Medical College, Cincinnati, 1919; formerly on the faculty of his alma mater; veteran of World War I; on the courtesy staff of the Franklin Boulevard Community Hospital, staff member at St. Bernard's Hospital, where he died Oct. 1, aged 62, of coronary occlusion.

Rogers, George McKinley, Philadelphia; Temple University School of Medicine, Philadelphia, 1921; died in the Lankenau Hospital Sept. 9, aged 59, of nephrosclerosis.

Shaffer, Stanley Norman, Forest Hills, N. Y.; Universität Bern Medizinische Fakultät, Switzerland, 1935; member of the American College of Chest Physicians and the American Trudeau Society; veteran of World War II; consultant on chest diseases to the New York City Health Department; attending physician at Triboro Hospital of Queens Hospital Center in Jamaica; died in the New York Hospital in New York City Sept. 16, aged 46, of coronary occlusion.

., Ansly Thomas ⊕ Edgerton, Wis.; College of Physicians Surgeons of Chicago, School of Medicine of the University Illinois, Chicago, 1907; veteran of World War I; on the staff of the Edgerton Memorial Community Hospital, where he died Sept. 3, aged 74, of cerebral thrombosis.

Sloan, George H., Mineral Point, Pa.; Cincinnati College of Medicine and Surgery, Cincinnati, 1885; died Sept. 4, aged 89, of carcinoma of the floor of the mouth.

Smith, Joseph ⊕ Greenville, N. C.; Medical College of Virginia, Richmond, 1914; died Sept. 23, aged 66.

Sparkman, Arthur Alphonzo ⊕ Thomasville, Ga.; College of Physicians and Surgeons, Memphis, Tenn., 1910; on the staff of the Veterans Administration; died in the Kennedy Veterans Administration Hospital, Memphis, Tenn., Sept. 14, aged 68, of carcinoma of the nasopharynx with metastases to the mediastinum, lung, and liver.

Spickschen, Henry F. ⊕ New York City; Ludwig-Maximilians-Universität Medizinische Fakultät, München, Bavaria, Germany, 1916; served on the staff of the Lenox Hill Hospital; died in Mexico City while on a vacation Sept. 30, aged 66.

Stacy, Archie Jackson ⊕ Tupelo, Miss.; Tulane University School of Medicine, New Orleans, 1918; specialist certified by the American Board of Radiology; served as secretary-treasurer of Northeast Mississippi Medical Society; member of the board of trustees of the Blue Mountain (Miss.) College; on the staff of the North Mississippi Community Hospital, where he died Sept. 29, aged 68, of coronary thrombosis.

Stickley, William Thomas ⊕ White Hall, Ill.; University of Illinois College of Medicine, Chicago, 1931; veteran of World War I; died Sept. 5, aged 58, of coronary disease.

Strobel, William George ⊕ Duluth, Minn.; Rush Medical College, Chicago, 1912; fellow of the American College of Surgeons; on the staffs of St. Luke's Hospital, Miller Memorial Hospital, and St. Mary's Hospital, where he died Sept. 20, aged 70, of acute myocardial infarction and hypertension.

Stroud, Homer Anderson ⊕ Jonesboro, Ark.; Memphis Hospital Medical College, Memphis, Tenn., 1903; fellow of the American College of Surgeons; formerly president of the Craighead County Medical Society, and vice-president of the Arkansas Medical Society; one of the founders and for many years president of the Craighead County Tuberculosis Association; chief of staff emeritus at St. Bernard's Hospital, where he died Oct. 1, aged 81, of paralysis agitans.

Thomson, Herbert Sedgefield, Corte Madera, Calif.; Johns Hopkins University School of Medicine, Baltimore, 1909; an associate member of the American Medical Association; formerly on the faculty of the University of California School of Medicine in San Francisco; veteran of World War I; served as chief surgeon of the Standard Oil Company; died Sept. 7, aged 73, of cancer of the esophagus.

Trapp, Anthony Nicholas ⊕ Chicago; Rush Medical College, Chicago, 1925; veteran of World War II; on the staff of St. Joseph Hospital, where he died Oct. 14, aged 59, of cerebral embolism.

Traugh, George Holton ⊕ Fairmont, W. Va.; University of Pittsburgh School of Medicine, Pittsburgh, 1919; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; past-president and secretary of the Marion County Medical Society; on the staff of the Fairmont General Hospital, where he died Sept. 19, aged 66, of coronary disease.

Vinsant, William Jonathan ⊕ San Benito, Texas; University of Tennessee College of Medicine, Memphis, 1900; member of the House of Delegates of the American Medical Association; on the staff of the Dolly Vinsant Memorial Hospital; died July 14, aged 82, of cerebral hemorrhage.

Ward, Thomas Leo ⊕ Arnolds Park, Iowa; State University of Iowa College of Medicine, Iowa City, 1926; member of the American Academy of General Practice; served as president of the school board; on the staffs of the Marcus Snyder Memorial Hospital in Spirit Lake and the Holy Family Hospital in Estherville; died Sept. 10, aged 59, of carcinoma of the bladder.

Willis, Hillary T., Hyattsville, Md.; University College of Medicine, Richmond, Va., 1898; five times mayor of Hyattsville; died in the Eugene Leland Memorial Hospital in Riverdale Sept. 12, aged 83.

Wright, John Bryan, Raleigh, N. C.; University College of Medicine, Richmond, Va., 1899; member of the Medical Society of the State of North Carolina; past-president of the Wake County Medical Society and the Raleigh Academy of Medicine; formerly member of the state board of health; on the staffs of the Mary Elizabeth Hospital, St. Agnes Hospital, and the Rex Hospital, where he died Sept. 29, aged 82, of a dissecting aneurysm.

Yarnell, Helen ⊕ New York City; College of Medical Evangelists, Loma Linda and Los Angeles, 1932; specialist certified by the American Board of Psychiatry and Neurology; certified by the National Board of Medical Examiners; member of the American Psychiatric Association; died in the French Hospital Sept. 8, aged 52, of Hodgkin's disease.

Yoder, Homer Maple ⊕ Smithville, Ohio; University of Wooster Medical Department, Cleveland, 1906; died Sept. 30, aged 83.

FOREIGN LETTERS

BRAZIL

Chlorpromazine in Psychiatry.—Dr. Spartaco Vizzotto and co-workers (*Arq. Depart. assist. psicopat.* 21:21, 1955) distinguish a "psychoplegic" action of chlorpromazine responsible for its effects on endogenous psychoses and a "neuroplegic" action of the drug related especially to cerebral circulation and edema. Observing the vessels of the fundus oculi during the injection of chlorpromazine intravenously, they noticed their reduction to about one-third of their original caliber. They interrupted a state of insulin coma with epinephrine and then investigated the influence of chlorpromazine. They concluded that the latter drug inhibits the action of the epinephrine. Although the authors do not claim that the result in their series of 71 cases is conclusive, it seems to confirm the favorable results reported in the literature on confusional psychoses of toxic or infectious origin in patients in whom anxiety predominates and in patients with status epilepticus or delirium tremens. In most patients with acute psychomotor excitement they obtained a tranquilizing effect but without remission of other symptoms, even in those who were affected only episodically. The symptoms of chronically excited patients were generally relieved to such an extent that they could return to their families. The authors also used chlorpromazine in patients with general paralysis who were intensely agitated and observed a prompt tranquilizing effect. In two patients who underwent a prolonged course of treatment with the drug, the spinal fluid used in the Wassermann reaction became entirely negative.

Schistosomal Cor Pulmonale and Myocarditis.—Dr. de Barros and co-workers (*Arquivos dos Hospitais da Santa Casa de São Paulo,* March, 1956) reported on two patients in whom cor pulmonale was a direct consequence of schistosomal infestation. The first patient had dyspnea, gallop rhythm, venous stasis, and tachycardia. The late stage of American trypanosomiasis had to be ruled out. The right bundle-branch block, as seen in the electrocardiogram, was also suggestive of trypanosomiasis. The presence of a generalized myocarditis with an eosinophil exudate explained the clinical and electrocardiographic similarities between the two diseases. In the second patient the pathologist's findings (intense pulmonary arteritis, arteriovenous fistulas, and generalized pulmonary sclerosis) explained the clinical manifestations. Ova were removed from the lumen by endothelial activity. The dissemination of the ova throughout the arterial circulation occurred through the arteriovenous fistulas and through the migration of ova from the arterial system into the pulmonary venous system through the loose intervascular connective tissue. Furthermore, the parasitic activity by means of ova was increased because they were laid in organs that normally do not constitute the habitat of the parasite. Adult male and female schistosomes were found in the brain and the heart. The severe involvement of the pulmonary arterioles explained the chronic cor pulmonale. The main cause of the hypertension was the serious arteritis, which was diffuse. This was an allergic reaction against the parasite and the ova. The eosinophil myocarditis had the same pathological background, the parasite and ova being found in the lungs and the heart.

Akinetic Mutism.—At the meeting on June 5, 1956, of the Associação Paulista de Medicina, Drs. Tenuto and Longman discussed two patients with akinetic mutism. One patient had a rhabdomyosarcoma in the left cerebellar hemisphere with bulbar compression. The other patient had a neurinoma in the left cerebellopontine angle, with atrophy by compression of the surrounding tissue. Akinetic mutism may be caused by rupture of the functional harmony of the brain through activation of an inhibitory mechanism in the cortex. According to this concept and based on modern neurophysiological research on the cerebellum, the authors admit that the lesions found in the cerebellum in the two cases reported may be responsible for the akinetic mutism through suppressive mechanisms located in the reticular system. They suggest, therefore, that the cerebellum may be included in the structural system, changes in which may cause akinetic mutism, which other authors have already connected with lesions in the mesencephalodiencephalic region and, at cortical levels, in the anterior part of the cingulate gyri.

Surgery in Children.—Dr. A. Amorim (*Rev. paulista med.* 49:61, 1956) investigated the metabolic rate in children and the meaning of its increase by such causes as pain and nervous instability. An adequate preanesthetic medicament helps to minimize the chances of shock and of nervous disturbances. Operation on infants requires great attention to details if serious complications are to be avoided. The loss of body heat, bleeding, and surgical trauma during an operation should be kept to a minimum. A child who is in a good state of hydration and nutrition and is free of respiratory or digestive diseases does not usually have any serious postoperative complications. Operative complications are due to poor surgical management or a poor general condition due to the disease itself. Water and electrolyte balance are of the utmost importance in the child. Alkalosis (a common complication due to continuous vomiting), acidosis, sodium and potassium deficiencies, and salt retention are hazards to be watched for.

Obstructive Jaundice.—At a staff meeting of the Medical School of the University of São Paulo, Dr. H. M. Sadek discussed obstructive jaundice. According to his experiments on dogs, there is a greater quantity of total direct-reacting bilirubin in the splenic, mesenteric, and renal veins than in the aorta. It is also greater in the infrahepatic than in the suprahepatic segment of the inferior vena cava. There is a greater quantity of late-reacting bilirubin in the mesenteric and renal veins than in the aorta and in the portal vein and infrahepatic inferior vena cava than in the suprahepatic vena cava. No changes in prompt-reacting bilirubin and indirect bilirubin in the first week of experimental obstructive jaundice were observed. In the spleen, intestines, and kidneys there is a greater quantity of total bilirubin and total direct-reacting bilirubin in the venous blood than in the arterial blood. In the liver the blood that leaves the organ has less direct-reacting bilirubin than the blood that enters it. Dr. Sadek admits the extrahepatic origin of bilirubin, which in no way disproves the liver's ability to form biliary pigment. His results suggest an intracellular production of bilirubin.

FRANCE

Colostrum Extract and Pituitary Gonadotropin.—R. Moreau and co-workers (*Presse méd.* 64:1545, 1956) gave a nonsaponifiable colostrum extract to mice but observed no change in them except for a slight loss of weight when large doses were given. In contrast to injections of estrogens, androgens, and progesterone, the injection of this extract had no gross effect on the genital tract of the immature mice. Histologically it caused some alterations in the epithelium, which assumed a mucosal appearance. The alterations are similar to but less marked than those obtained with large doses of androgens. After saturation with the colostrum extract, the injection of estrone or progesterone promotes an increase in the weight of the uterus, but the extract seems to potentiate only the action of estrogens and not that of progesterone. In no case is there any inhibiting effect. In animals treated with colostrum extract, then injected with pituitary gonadotropin, the phenomena proper to this hormone are not observed; specifically there is no increase in the weight of the uterus and no keratinization of the vagina. Romani and Quantius, using virgin does, believe the appearance of a hemorrhagic follicle to be a positive test for the follicle-stimulating hormone. This test is rendered negative by the injection of a sterolic extract of colostrum. The extract appeared to inhibit the response of the ovarian receptor to the pituitary stimulation.

The items in these letters are contributed by regular correspondents in the various foreign countries.

Lung Cancer.—G. Brouet and co-workers (*Presse méd.* 64:1548, 1956) report that alveolar carcinoma of the lung is a rare form of intrathoracic tumor. They observed a case in a 55-year-old woman whose clinical symptoms first appeared eight years before she died. In her last years she had a profuse bronchorrhea, with expectoration of more than 1 qt. of sputum a day. The authors point out that certain cases of intractable bronchorrhea that have been previously reported might have been associated with an unrecognized alveolar epithelioma. In the authors' case, no extrathoracic tumor was found, thus excluding the possibility of its being metastatic in origin.

Bone Lacunas in the Cranial Vault.—P. Wertheimer and co-workers (*Presse méd.* 64:1556, 1956) report that bone lacunas in the cranial vault may be classified in the following ways: (1) traumatic congenital; (2) inflammatory due to syphilis, tuberculosis, osteomyelitis, or a mycosis; (3) due to a primary tumor, benign tumor, metastatic tumor, or neighboring tumor, such as a meningioma; (4) due to diseases of the hematopoietic system, such as myeloma, chloroma, Hodgkin's disease, and various anemias; (5) due to bone dysplasia (reticulosis, such as lipoid granulomatosis or xanthomatosis, eosinophilic granuloma, Paget's circumscribed osteoporosis, Jaffe and Lichtenstein's dysplasia, or fibrous osteitis); (6) endocrine osteoses, such as parathyroid fibrocystic osteosis, exophthalmic goiter, pituitary basophilism, Milkman's syndrome, and postmenopausal osteoporosis; and (7) cysts in the cranial vault associated with multiple neurofibromatosis. Because there are so many causes, the diagnosis cannot be made on the basis of the reading of the roentgenogram alone.

Chemotherapy of Tuberculosis.—Pestel and Ravina (*Presse méd.* 64:1577, 1956) stated that certain advantages derive from adding drugs with an anti-inflammatory action to those specifically antibacterial agents commonly used. Both phenylbutazone and aminopyrine with phenylbutazone proved particularly effective in this respect because of their practically constant control of the inflammatory reactions of tuberculosis. The authors, by giving equal amounts of isoniazid and phenylbutazone simultaneously, obtained remarkable results in the treatment of erythema nodosum, primary tuberculosis, and serofibrinous pleurisy. This treatment was well tolerated.

Tetracycline and Experimental Infections.—J. C. Levaditi and co-workers (*Presse méd.* 64:1579, 1956) treated repeated experimental infections in mice induced by intraperitoneal injections of cultures of Salmonella typhosa, Escherichia coli, *Diplococcus pneumoniae*, or Micrococcus pyogenes var. aureus with tetracycline. The infections were well tolerated in spite of their being repeatedly induced. Although the strains used were virulent, many animals developed a resistance to infection as a result of repeated contact and antibiotic treatment. The time required for the appearance of this resistance as well as its duration varied with the bacterial species used and with the individual mouse. In some of the mice the acquired resistance persisted and in others it disappeared rapidly. Similar reactions are observed when streptomycin is used in place of tetracycline.

PERU

Chlorpromazine and Mental Diseases.—Although chlorpromazine is not a specific cure for the psychoses, it is one of the most important tools of modern psychiatry for the management of mental diseases, and, when used with insulin and/or electroshock therapy, it renders the therapeutic results more satisfactory than does any other form of treatment, according to Drs. M. Querol and M. Chicata, of the National University of San Marcos, in an address before one of the meetings of the centennial celebration of the Faculty of Medicine of Lima. They compared the therapeutic results in groups of schizophrenic patients. In the series in which chlorpromazine was given alone or with electroshock therapy, 98% of the patients were benefited in some degree, whereas in the groups treated otherwise only 71% were benefited, despite the number of patients in whom the disease was of shorter duration than in the former. The best results were observed when chlorpromazine was combined with insulin. The authors advance the hypothesis that the therapeutic effects of shock therapy and chlorpromazine reinforce each other. They gave chlorpromazine to 50 patients with schizophrenia, 12 with manic-depressive psychosis, and 9 with chronic alcoholic psychosis. Therapy was started with minimal dosage, which varied according to the severity of the disease, and was slowly increased until the optimal dosage was reached. This dosage was maintained for a variable period suitable to permit the best clinical response, and then it was reduced gradually to the minimal maintenance dose. All patients received chlorpromazine by mouth, but those showing great agitation were given the drug intramuscularly for the first few days.

In the group of schizophrenic patients about 90% of those who had had the disease more than a year had previously failed to respond to other forms of treatment. Only those patients unresponsive or unsuitable for shock therapy were considered in the first trial, but the strikingly favorable results obtained in these patients encouraged the authors to use chlorpromazine in patients who had had no previous treatment. The period of active treatment, from the onset of the therapy to the establishment of the maintenance dose, ranged from 24 to 261 days. The average maintenance dose was 100 mg. daily. The drug was given alone in 26 patients and with shock therapy in the rest. Promethazine hydrochloride and barbiturates were given to induce sleep in some patients in whom insomnia paradoxically followed the administration of chlorpromazine or if the patient had to be given the drug for a long time. Promethazine and stramonium powders proved useful in diminishing or preventing the paralysis agitans induced by chlorpromazine. Promethazine also prevented skin eruptions, which, when present, were in no case severe enough to warrant the discontinuance of the therapy. In nine disturbed and agitated patients, reserpine was given as an adjuvant in doses of from 1 to 4 mg. daily over a mean period of one month. Vitamins, particularly of the B complex, and mild laxatives were given routinely. In the group of patients who had had the disease one year or less, 85% obtained a total remission and 15% a social remission, whereas in the group of patients who had had the disease more than a year, only 24% obtained a total remission, in 32% there was a social remission, in 35% slight improvement, in 3% no improvement, and 6% died. Patients with the paranoid, catatonic, and paranoid-catatonic types of schizoprenia showed the best results. Chlorpromazine definitely proved more beneficial when used with shock therapy than when used alone.

The tranquilizing effect of the drug was especially striking, the agitation subsided generally within the first week of therapy, and both anxiety and psychomotor hyperactivity were greatly reduced. Some morbid states, such as fear and anguish, yielded to the drug long before mental disturbances of psychic spheres other than the affect responded. The patients became better aware of their environment and became accessible for concurrent psychotherapy. Hallucinations became less severe in the fourth to sixth week of therapy, but disturbed ideation was found to be the symptom most resistant to treatment. Late in the course of the treatment the improved patients began to realize the unreality of their delusions. Some patients had no memory for the delusions they harbored during their period of agitation. From the first days of treatment slowness of motion was noticed in several patients. Amimia and involuntary movements were not unusual findings, and a reversible paralysis agitans–like syndrome was observed in 64% of the patients in the series. Late in the course of the treatment, seven patients showed melanoid hyperpigmentation of the face; four, clouding of the consciousness, four, vomiting and diarrhea; two, acute pneumonopathy, two, unexplained fever, one, muscular atrophy; and one, edema

Two patients died during the trial. One of these was in the fourth month of therapy and at that time was taking 500 mg. of chlorpromazine and 4 mg. of reserpine daily. He showed a frank paralysis agitans–like syndrome. Suddenly he developed a high fever and went into shock. His medication was stopped at once, but he died two days later. Chlorpromazine was thought to be the immediate cause of death in this patient; but, in the other, bronchopneumonia and anasarca occurring at the end of the second week of treatment caused the death. Of the 38 patients who were discharged from the hospital, only 18 could be followed up. In 16 of them the remission lasted 2 to 12 months. Several were, when last seen, still receiving the daily maintenance dose under close medical supervision. The other two patients relapsed, one after a month and one after a year outside the hospital. Active therapy must be continued for 2 to 4 months and the maintenance dose taken for an indefinite period in order to prevent relapses. It is likely that larger doses than those used thus far can be given for prolonged periods with even better results than those reported.

As regards the patients with manic-depressive psychosis, seven were in the manic phase and five in the depressed phase. The time elapsed between the onset of the current phase and the beginning of the treatment ranged from 15 days to 4 months in the former and from 3 to 8 months in the latter. The duration of active therapy was 12 to 68 days for those in the manic phase and from 48 to 128 days for those in the depressed phase. The optimal dosage was 100 to 500 mg. daily in the first group and 25 to 300 mg. daily in the second group. In three manic patients, electroshock therapy was also used; this treatment was also used on all patients in the depressed phase. The results were dramatic in the manic patients. All recovered completely except two who died from causes not attributable to chlorpromazine. The mental symptoms improved earlier than in the schizophrenic patients. Within a month of the beginning of therapy almost all the symptoms had subsided. In one patient in whom the medication was abruptly stopped the symptoms returned but subsided again when therapy was resumed. Although in the depressed patients the symptoms subsided within 30 to 60 days of starting therapy, the authors belive that in these patients chlorpromazine acts as an adjuvant to electroshock therapy.

In the alcoholic patients the duration of the psychosis varied from 15 days to 4 months. Active therapy was given for 10 to 45 days, and in no patient was maintenance treatment required. The daily dose ranged from 50 to 200 mg. All the patients were given vitamins and lipotropic agents. In three, electroshock therapy was also used. Complete remission of the psychosis was observed in all the patients. The favorable effect of the drug on tremors was particularly striking.

Radioactive Iodine in Hyperthyroidism.—At the same meeting Drs. J. Correa and F. Moncloa, of the Arzobispo Loayza Hospital of Lima, reported that radioactive iodine is a safe, effective, inexpensive therapeutic agent for patients with hyperthyroidism. In their series of 30 patients treated with this agent, three had previously undergone a thyroidectomy that failed to cure the disease. A single dose of I^{131}, varying from 4 to 15 mc., was given to all patients. Three patients were observed for more than 6 months, 7 for three months, 8 for two and a half months, and 12 for one month or less. The disease was completely arrested in the three patients of the first group, one of whom showed mild transient signs of hypothyroidism. In the second group, five patients became euthyroid and the other two, although improved, still showed slight manifestations of hyperthyroidism. In the third group, two were cured, five were improved, and the remaining one was thought to need another dose of I^{131}. In the fourth group, the follow-up period was too short to justify any conclusions, but significant relief of symptoms was observed in all. In none of the patients whose disease was completely arrested by I^{131} has a relapse been reported. The authors believe that in the patients treated with I^{131} complete control of the hyperthyroidism does not occur in less than three months after the first dose. For this reason a second dose of I^{131} should never be given after the first dose.

Infertility.—At the same meeting Didedle and Tietze stated that in 86% of normal couples pregnancy occurs in the first year of marriage and in 95% it occurs in the first two years. It is generally believed that the age of the wife plays an important role in fecundation and that her chances of becoming pregnant early in the course of marriage diminish as she grows older. A report concerning 160 infertile couples was presented by Dr. Carlos Muñoz T. In all cases the cause of the sterility was determined. Obstruction or occlusion of the oviducts was present in 49.36%. This high incidence of tubal lesions was probably due to the fact that the author's series included only hospital patients, in whom gonococcic postabortive and postpartum infections are common. In 375 insufflations on these patients, 15 being the greatest number made on any one patient, there were no complications; 12 of 79 patients in this group subsequently became pregnant. In 28 women, or 17.5%, an ovarian factor was found to account for the sterility. Disturbances of the follicular phase were found in 18 of them, and 10 had a faulty progestational phase. Thyroid dysfunction was found in 11 patients, who showed either frank signs of hypothyroidism or subclinical hypothyroidism (a basal metabolic rate of about—10, a blood cholesterol level close to the maximal normal value, and a sterility counteracted by thyroid extract). In two patients the urinary 17-ketosteroids were found to be increased. Seven patients, or 25.9%, became pregnant after proper treatment.

A cervical factor was thought to play an important role in the sterility in 18 women, or 11.25%. In seven of them pregnancy followed adequate therapy. Genital tuberculosis was found in 9 patients, in all of whom the course of the disease had been insidious and evidence of tuberculosis in other organs had been lacking. The diagnosis was made by means of endometrial biopsy. Congenital malformations were found in two patients, uterine myoma in two, a large dermoid ovarian cyst in one, and a bilateral tubo-ovarian endometriosis in one. In 20 cases it was the husband who was sterile. In the 77 husbands examined, 55 had normal sperms, 18 had defective sperms, and 4 had no sperms in their seminal fluid.

Mitral Stenosis.—At the same meeting Dr. G. Whittembury and co-workers reported that no systematic increase in the proportionate amount of blood contained in the lungs arises in mitral stenosis. Their study included 4 men and 16 women. In seven patients the stenosis was grade 2, in six it was grade 3, and in seven grade 4. Operation verified the diagnosis in six of the patients, none of whom showed mitral insufficiency. The circulation time, cardiac index, pulmonary blood volume, intrathoracic blood volume, and total blood volume of these patients were compared with those of normal persons. All patients were studied in basal conditions after a rest of at least 45 minutes. It was found that the circulation time increases, the cardiac index decreases, and the blood volume increases with the increasing severity of the disease. Mean values of the circulation time showed almost equivalent variations in patients with grade 2 and 3 stenosis but were significantly less in those with grade 4 stenosis. No difference was observed between the cardiac index of those with grade 2 and 3 stenosis, but this index was significantly lower than in patients with grade 4 stenosis. The difference between the normal values of total blood volume and those of patients with grade 2 stenosis was not significant, but the volume was less than that of those with grade 3 stenosis and much less than that of patients with grade 4 stenosis. Expressed as absolute values the increase of the pulmonary blood volume paralleled the severity of the disease, but expressed as a percentage of the total blood volume the increase was only significant in patients with grade 3 stenosis. Although the values of the intrathoracic blood volume tended to increase with the severity of the disease, the difference between the mean values of normal subjects and of patients with mitral stenosis was not statistically significant. A statistically significant correlation was found between pulmonary blood volume and intrathoracic blood volume.

Acute Failure of the Left Ventricle.—At the same meeting Dr. Victor Alzamora Castro, head of the department of cardiology of the Dos de Mayo Hospital, recommended massage of the carotid sinus in patients with acute insufficiency of the left ventricle associated with hypertension. He used this treatment in a series of 31 patients and brought the crisis under control in 26. In some patients the response was prompt and dramatic, consisting of alleviation of the pulmonary signs, relief of dyspnea, and diminution of the intensity of the heart sounds within the first minutes of the massage. Shortly after the maneuver some patients became tranquil and could lie supine. At first no other therapy was used, but later morphine and/or digitalis were given to those patients who seemed to need such a medicament. Amobarbital was also given to very hypertensive patients. The massage, however, appeared to do more good than the drugs. In general the beneficial effect of the massage becomes manifest a few seconds after it is started. A great advantage of the procedure is that the physician can control the intensity of the changes of cardiac frequency and blood pressure. In some patients arterial hypotension was induced in 30 minutes, and it is believed that this response could be maintained as long as the massage was used. No accidents occurred in the author's series of patients, but the massage should always be gentle.

The procedure failed to control the condition in two patients with auricular fibrillation and three with aortic insufficiency. In these conditions the massage has proved to be generally ineffective. In one patient with auricular flutter the treatment was successful. In two patients with pulmonary edema, mitral stenosis, and hypertension it averted the crisis. In patients with acute failure associated with arterial hypotension the procedure is contraindicated. The fall in blood pressure and the decrease in cardiac work that are thought to follow the peripheral vasodilatation induced by massage have been achieved by some physicians through ganglion-blocking agents, but the difficulty in controlling the results and the danger of causing too great a drop in blood pressure make their use hazardous. This treatment seems also to benefit patients with angina pectoris and even those with coronary occlusion. Prolonged massage of the carotid sinus shortens the duration of the fatigue in cardiac patients undergoing physical effort tests.

UNITED KINGDOM

Cortisone in Chronic Asthma.—The subcommittee on Clinical Trials in Asthma of the Medical Research Committee has issued a report of a controlled trial of the effects of cortisone in the treatment of chronic asthma and status asthmaticus. The trial on chronic asthma was carried out in six centers in the United Kingdom, in which 96 patients received either cortisone or placebo tablets. Those included in the trial were between 40 and 60 years of age, had a history of asthma of not less than three months' duration, and had had no complete remission of more than two weeks in the preceding three months. Patients with severe bronchopulmonary infection or a history of cardiac failure or tuberculosis were excluded from the trial. Each patient treated with cortisone received 300 mg. the first day of the trial, 200 mg. on the second and third days, and 100 mg. daily for the next four days; subsequently the dose was adjusted according to the requirements of the patient. All patients were treated for 24 weeks and followed up for a further 12 weeks, during which an attempt was made to withdraw the cortisone. In addition, each patient received any antispasmodic therapy considered necessary. The patients' condition was evaluated before and after treatment by physical examination, exercise tolerance, ability to work, and vital capacity. At first, slight but definite benefits were observed in the patients treated with cortisone, particularly diminution of rhonchi and increased exercise tolerance during the first eight weeks of treatment. By the end of 24 weeks and during the three months' follow-up study, the control patients gained ground, with the result that at the end of this period there was little difference between the two groups. The use of cortisone showed no advantage in enabling those to work who were initially unable to do so. The changes in vital capacity showed wide and similar variations in both groups. The general impression was that 23 of the 49 patients treated with cortisone were improved as compared with 12 of the 47 patients receiving the placebo.

The 32 patients included in the trial of the effects of cortisone in the treatment of status asthmaticus were all more than 14 years of age, had had at least one previous severe attack of asthma, and had not received any cortisone previously. All were admitted to the hospital and given what was the standard treatment in that hospital (e. g. epinephrine isoproterenol sulfate, aminophylline, and oxygen). Patients remaining in status asthmaticus after 24 hours of treatment were admitted to the trial. On the first day 350 mg. of cortisone was given in divided doses, on the second day 200 mg., then the dosage was reduced by 25 mg. daily until the 10th day, when no cortisone or placebo tablets were given. The total amount of cortisone administered was 1.25 gm. Clinical evaluation was based on a determination of the degree of bronchial obstruction present, using five arbitrarily defined clinical grades, and on temperature, respirations, and pulse rate. Details were also noted of antispasmodics used. The patients in the group treated with cortisone, without doubt, fared better than those in the control group. By the fourth day of treatment, 10 of the 15 patients treated with cortisone no longer had disabling bronchial obstruction, whereas only 4 of the 17 patients in the control group were as well as these patients. This difference between the two groups was maintained to the end of the period of treatment. Observation of the patients for three months after the trial showed that those in both groups reverted to their usual asthmatic condition. In the opinion of the committee, unless the patient is exhausted and dehydrated, cortisone should be used only when other methods used for 24 hours have failed.

"Prescribers' Notes."—The current issue of *Prescribers' Notes* sent to physicians in the National Health Service warns against the dangers of the indiscriminate use of erythromycin. It states that, because of the development of resistance of micrococci to the drug, it should be used only when the organisms have become resistant to penicillin and other antibiotics, and not as the first line of defense. It should not be used for chronic or trivial conditions and when the bacterial cause of an infection is not known. Attention is also drawn to the misuse of cortisone in the treatment of rheumatoid arthritis. The subcommittee of the Empire Rheumatism Council is quoted as finding no significant difference, after one year's treatment, between the two similar groups of patients, one treated with aspirin and the other with cortisone. *Lancet,* commenting on this report, notes: "Meanwhile the evidence from this and earlier trials raises the question whether cortisone, with its acknowledged dangers, is ever indicated in rheumatoid arthritis." Economy in prescribing is urged. The prices of various analgesics are compared with that of aspirin. Panadol (N-acetyl-p-aminophenol), which has the same analgesic action as acetophenetidin, costs three times as much as aspirin. One proprietary preparation of codeine compound is, on the other hand, only a few cents more a pack than the patented preparation. Figures are cited showing the large increase in the prescribing of proprietary preparations. In 1950, of the total number of prescriptions issued, 18% were for proprietary preparations; in 1955, 36% were.

Dangers of Myelography.—The dangers to the patient of myelography are pointed out by Davies (*Lancet* 2:747, 1956), who followed up 119 patients subjected to this procedure for periods of from 1 to 15 years. All but one have received injections of iophendylate, and 70 patients had experienced abnormal reactions to the injection. Complaints included headache, nausea, vomiting, giddiness, an increase in the severity of the original neurological symptoms, meningism, cranial nerve palsy, nystagmus, retention of urine, pyrexia, and severe pain in the spine. Fourteen patients had chronic symptoms or disabilities persisting for a year or more. These included headache, cervical pain and stiffness, persistent backache, continuous pain and cramp in the legs, urinary incontinence, intercostal neuralgia, paresthesias, and intensification of the original symptoms. The contrast agent was detected in the subarachnoid spaces of the brain and spinal cord two years after myelography. This was confirmed postoperatively, radiologically, and at autopsy on those who died. Davies considers that myelography should never be performed unless absolutely necessary and that, if it is, as much of the contrast agent as possible should be removed after the examination.

Malignant Hypertension and Irradiation.—A case of malignant hypertension induced by the irradiation of one kidney is described by Levitt and Oram (*Brit. M. J.* 2:910, 1956). A man had his left testis removed for seminoma, and, since secondary deposits formed in the upper abdomen, he was given deep roentgen therapy (3,000 r) to the left renal region. Later his blood pressure rose from 150/90 mm. Hg to 215/130 mm. Hg, with corresponding hypertensive changes in the electrocardiogram, while ophthalmoscopy revealed retinopathy grade 3 to 4. The process suggested a relatively acute and recent condition. Radiography showed an enlarged left ventricle and a poorly functioning left kidney. The latter was eventually removed. The blood pressure fell and all symptoms disappeared after the nephrectomy. Within 10 months there was no retinopathy. The case is of interest in view of Goldblatt's researches and the role of unilateral renal disease in causing hypertension.

Effect of Cortisone.—The *British Medical Journal* (2:800, 1956) contains a report by Dr. T. Nicol and co-workers on animal experiments that indicate that cortisone lowers the body defenses by depressing the phagocytic activity of the reticuloendothelial system, the total and differential leukocyte counts in the blood, and the gamma globulin level in the serum. Its beneficial action in certain diseases is probably due to a similar mechanism whereby it depresses the inflammatory reaction of the patient and thus holds in check the cycle of pathological changes. This is well illustrated in the cases of tenosynovitis and iridocyclitis, in which the use of cortisone reduces the inflammatory response and prevents the formation of adhesions while the infecting organisms can be attacked therapeutically with antibiotics. It would seem desirable, whenever possible, to give cortisone locally rather than systemically, in order to limit the depression of the defense mechanisms.

Calling the Resident.—In July St. Thomas's Hospital installed a new magnetic system for quickly summoning residents from anywhere in the hospital. It replaces the bells formerly used and at a lower cost for installation and upkeep. The system is based on that used for transmitting simultaneous translations of speeches at international congresses. Each member of the staff on call is provided with a receiver, resembling somewhat the handle of a small ophthalmoscope, which is clipped into a pocket. Each receiver—up to 56 can be run on one circuit—responds only to a signal from the controlling transmitter given at its own frequency. The response is a low-tone "peep, peep." With slight modification, the receiver can be adapted to transmit the human voice, but at St. Thomas's a nonverbal signal is preferred. The adaptation has been highly successful and is described in the October issue of *Hospital* (London).

Health Service Aims.—The annual report of the Ministry of Health for 1955 states that high priority will be given to bringing existing hospitals to a satisfactory standard and to providing new accommodation as and where it is needed; to insuring that the mental health services receive a proper share of the new construction and other resources available; and to providing adequate care for older persons. The achievement of these objectives will be facilitated by the rapid curtailment in the need for special beds for patients with tuberculosis.

A Fluorine-Containing Anesthetic.—Fluothane is a new fluorine-containing anesthetic that is being developed here. Bryce-Smith and O'Brien (*Brit. M. J.* 2:969, 1956) state that it is noninflammable and nonexplosive in the presence of 50% oxygen, undecomposed by warm soda lime (unlike trichloroethylene), and nonirritating to the respiratory mucosa and that it produces rapid anesthesia with quick recovery unaccompanied by nausea or vomiting. They administered fluothane by the open drop method, with the use of an inhaler calibrated to deliver known concentrations of fluothane vapor in air. A 2 or 3% concentration of fluothane in air produced a satisfactory level of surgical anesthesia after light premedication with meperidine hydrochloride or Pantopon and induction with thiopental sodium. Among the undesirable effects of fluothane were bradycardia, hypotension (average 90 mm. Hg systolic), and respiratory depression independent of the rate and depth of anesthesia. Cyanosis was frequently seen unless respiration was assisted or oxygen added to the gas mixture. Respiration was usually smooth and quiet, and regular muscular relaxation was generally sufficient; but, as the number of upper abdominal operations in this series was restricted, further information on this is needed. Some patients were also given muscle relaxant drugs, but the use of these with fluothane sometimes resulted in a severe fall in blood pressure. Recovery from the anesthetic usually occurred within 10 minutes after the stopping of its administration. The greatest disadvantage of fluothane was the depression of respiration; this was sufficient to limit its use to trained hospital anesthetists.

Excessive Prescribing of Cortisone.—Dr. T. Wilson, addressing a local hospital management committee at Bridlington, Yorkshire, said physicians were wasting the public money by prescribing cortisone too lavishly to patients with rheumatoid arthritis. He said that when patients went to consultants they received as much as three or four months' supply of the drug, which is very expensive. On an average a three months' supply costs $50; in some cases patients were receiving as many as 500 tablets at a time, costing $150. As some patients stopped taking the drug after a time, this represented a great waste. Dr. Wilson urged economy in prescribing such expensive preparations. Smaller supplies could be prescribed and then renewed when necessary. He also referred to the overspending of $8,700 on drugs and dressings at a local hospital, where the monthly consumption of cortisone was $1,625 against an estimated requirement of $300. A 2-oz. tube of hydrocortisone ointment costing $20 was often given to hospital patients for use as if it were calamine cream.

Dangers of Frozen Eggs.—Dr. K. E. Hughes, director of Portsmouth public health laboratory, addressing a meeting of the Royal Society of Health, described the importation of frozen eggs without control of their processing or sterilization before use as a grave menace to health. He said that large quantities of foreign frozen eggs were imported into the United Kingdom and that many of the eggs contained Salmonella. He said that of the last 171 batches of eggs examined at Portsmouth 44% were infected. If an infected batch were put through a baking process that did not kill the organisms, infection could result. He also said that synthetic cream was dangerous and had been the cause of outbreaks of salmonellosis. Another health officer, Dr. S. Hewitt, said that many outbreaks of food poisoning go unreported.

New Surgical Dressing.—A new microporous film wound dressing has been developed by Scales and co-workers (*Brit. M. J.* 2:962, 1956) from polyvinyl chloride film, with the use of polypropylene sebacate as a plasticizer. The film is manufactured by incorporating a pore-forming ingredient, such as starch or salt, into the plastic mass before its extrusion as a sheet. The pore-forming agent is later removed, leaving a structure whose porosity depends on the number and size of the intercommunicating pores between the cavities. This film is permeable to water vapor but not to bacteria contained in an aqueous medium. Trials were made to compare the healing rate of minor injuries covered with the new dressing with that of a similar group of minor injuries protected with a standard water-proof occlusive dressing. The new dressing largely fulfills the properties of an ideal dressing, namely, a high porosity to water vapor, absorption of blood and exudate, exclusion of micro-organisms, and being unaffected by domestic or industrial fluids, noninflammable, easily sterilized, and capable of being sealed to the skin. The film has a porosity of 1,400 to 1,800 gm. of water vapor per square meter at 37 C when the relative humidity is 75%. One drawback of the new dressing is that it is adherent to the wound surface.

Dickens' Illnesses.—The medical history of Charles Dickens, who was a chronic invalid, is discussed by Dr. W. H. Bowen in his book "Charles Dickens and His Family," published by N. Heffer and Sons, Ltd., Cambridge, England. Dickens, who died at the age of 58, is said to have suffered from renal calculi, chronic renal disease, gout, anal fistula, and cerebral atheroma. These conditions were diagnosed in retrospect by Dr. Bowen from a study of letters and contemporary documents. The novelist consulted Sir Henry Thompson in 1867 about his toe; erysipelas over an inflamed bunion was the diagnosis. In 1869 the diagnosis of gout was considered, but this was dismissed by Syme of Edinburgh, who confirmed the diagnosis of an inflamed bunion. When the first symptoms of cerebral atherosclerosis appeared, Dickens consulted Sir Thomas Watson and the advisability of discontinuing his public readings arose. Dickens' readings of his works were extremely popular, and Sir Thomas Watson agreed that they might continue without detriment to his health.

A New Steroid.—A new steroid found in chloroform extracts of human urine and related to mineral metabolism was described by Prunty and co-workers (*Lancet* 2:925, 1956). As it was first detected in the urine of a patient named Wildego, it has been provisionally called wildegosterone. It is distinct from aldosterone and has been identified by its ultraviolet absorption spectrum after separation by chromatography. The new steroid has not been found in the urine of healthy persons on a normal diet but only in the urine of patients with edema and muscle weakness or in that of normal persons after the administration of potassium ions. In an investigation of adrenal function in 100 pregnant women, the excretion of wildegosterone was found to increase steadily as pregnancy progressed, both in normal women and in those with toxemia. The findings suggest that wildegosterone is related to the metabolism of water and electrolytes.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Factors Influencing Conversion of Chronic Atrial Fibrillation with Special Reference to Serum Quinidine Concentration. M. Sokolow and R. E. Ball. Circulation 14:568-583 (Oct.) 1956 [New York].

Conversion of chronic atrial fibrillation or flutter to sinus rhythm was attempted 214 times in 177 patients, 94 of whom had rheumatic heart disease, 38 coronary heart disease, 20 hypertensive cardiovascular disease, 10 thyrotoxic heart disease, 1 congenital heart disease, and 14 miscellaneous conditions. One hundred fifty-three of the attempts were successful, and 61 were failures. Eight of the 177 patients had chronic atrial flutter and 169 had atrial fibrillation. Successful conversion of atrial flutter to sinus rhythm with quinidine was achieved in five patients, and in the three others the attempt failed; successful conversion of atrial fibrillation to sinus rhythm was achieved in 125 of the 169 patients. Thus successful conversion was achieved in 74% of the total group, but the percentage varied depending on the causation, duration of the fibrillation, presence of cardiac failure, and, in the patients with rheumatic heart disease, the type of the valve lesion. Atrial fibrillation of more than six months' duration decreased the likelihood of conversion in both the rheumatic and nonrheumatic patients. The incidence of conversion can be as high as 95% in nonrheumatic patients with fibrillation of short duration and as low as 45% in patients with rheumatic mitral incompetence with fibrillation of more than a year's duration. In the group with rheumatic heart disease, the poorest results were obtained in patients with predominant mitral incompetence, even when the effects of duration and presence of cardiac failure were excluded. In patients with uncomplicated mitral stenosis or with predominant aortic valvular disease the rate of conversion was almost as high as that in the nonrheumatic group. The presence of cardiac failure decreased the likelihood of successful conversion. The presence of systemic emboli in the immediate or remote past did not interfere with successful conversion of atrial fibrillation.

The average serum quinidine concentration required for conversion was 6.1 mcg. per cubic centimeter This level was achieved with an average dose of 2.2 gm. daily. Eighty per cent of the successful conversions were accomplished with a daily dose of 3 gm. or less of quinidine. With increasing doses, the additional yield of conversions without toxicity requiring cessation of the drug was only 20%. Eighty-five per cent of the successful conversions occurred at serum concentrations of 8 mcg. per cubic centimeter or less. Myocardial toxicity was infrequent at serum concentrations of less than 6 mcg. per cubic centimeter, but progressively increased as the serum concentration exceeded this figure. Toxicity was not always correlated with high serum levels, since 7 instances of myocardial toxicity were observed in 429 observations at levels of less than 6 mcg. per cubic centimeter. Caution must, therefore, be exercised, even when serum concentrations are low or falling. Toxicity was related more closely to the serum quinidine concentration than to the daily dose of the drug. A wide individual variation in serum concentrations was observed in patients receiving the same dose of quinidine.

The use of quinidine in established atrial fibrillation should be considered a calculated risk, and the physician must weigh the potential benefits against the possible hazards. Caution and reconsideration of the total situation should be the rule when 3 gm. of quinidine per day does not effect conversion or when the serum concentration reaches 8 mcg. per cubic centimeter Control of therapy with knowledge of the serum quinidine concentration should decrease the risk by indicating the statistical likelihood of toxicity at increasing concentrations of the drug Relapses to atrial fibrillation occurred in 85% of patients who did not receive maintenance doses of quinidine, but in only 20% of those given a maintenance dose of 1.6 gm. per day or in whom the maintenance serum concentration was more than 60% of the peak conversion serum level. The changing patterns of the atrial arrhythmia with increasing doses of quinidine and progressive slowing of the atrial rate support the concept that atrial fibrillation, atrial flutter, and atrial tachycardia are different manifestations of an ectopic focus and that the electrocardiographic differences between the three arrhythmias are a function of the atrial rate (rate of discharge of the atrial ectopic focus)

Febrile Pseudorheumatic Types of Early Cancer. I. Aguilar Rodríguez. Rev. clín. españ. 61:370-374 (June 30) 1956 (In Spanish [Madrid, Spain].

Febrile pseudorheumatic types of early cancer are frequent. The symptoms consist of fever and arthralgia of the type of acute polyarticular rheumatism Pain involves the ankles, shoulders, knees, and wrist joints. It can be differentiated from polyneuritis and the local pain caused by cancer or from its metastases. The joints may be inflammed and even deformed The etiology of the febrile type is difficult to interpret. Fever is high and resistant to antipyretic treatment. Arthralgia does not respond to antirheumatic treatment. Roentgen examination of the involved joints shows no metastases. Thirty-six patients with the typical syndrome were observed. Nine representative cases are reported. There were neither clinical symptoms nor roentgen signs of cancer in any patient. The erythrocyte sedimentation rate was accelerated. Symptoms followed the typical pattern in all cases. They either progressed to the state of anorexia, asthenia, symptoms of general infection, loss of weight, and appearance of the tumor in a few weeks or a few months, or they subsided temporarily and reappeared to follow the same course. A diagnosis of cancer was made only by the appearance of the tumor, which was noted several weeks or a few months after the appearance of the febrile pseudorheumatic symptoms The tumor was located in the stomach in 22 patients, either in the liver or in the lung in 4 patients, in the rectum in 2, in the pancreas in 1, in the kidney and brain in 1, in the bladder in 1, and in the cecum in 1. These types of cancer constitute an adaptation syndrome (according to Selye). They are due to an imbalance of the suprarenal hormones from a stimulus of the suprarenal glands under effect of cancerogenic substances Cancer of these forms is highly malignant. It runs a rapid course to a fatal end.

Syndrome of Congenital Absence of the Spleen with Associated Cardiovascular and Gastroenteric Anomalies. M. J. Aguilar, H B Stephens and J. T. Crane. Circulation 14:520-531 (Oct.) 1956 [New York].

Twenty-seven cases of congenital absence of the spleen in infants were collected from the literature, and three recent additional cases in a 20-month-old white baby girl and in two Chinese infants aged 3 months and 5 days, respectively, with certain cardiovascular and gastrointestinal abnormalities are reported. The three infants died, and autopsies revealed a characteristic association of multiple congenital anomalies, such as septal defects, particularly communication through a common atrioventricular orifice, anomalous venous return to the heart, pulmonary stenosis or atresia, transposition of the great vessels, accessory lobes of the lungs, partial situs inversus of the abdominal viscera, and abnormal mesenteric attachments. A complete blood cell count was done in two of the patients and revealed certain abnormalities, such as the presence of target cells

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The place of publication of the periodicals appears in brackets preceding each abstract.

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The presence of agenesis of the spleen presents extremely valuable information to the cardiovascular surgeon, especially as the cardiac anomalies often follow a predictable pattern. Having found partial situs inversus of the abdominal viscera in a patient showing the hematological abnormalities cited above, one should then strongly suspect the associated congenital heart disease to be of the cor biloculare type with a common atrioventricular orifice, anomalous venous return to the heart, and pulmonary stenosis or atresia. Less frequently there will also be present abnormalities of the great vessels, such as transposition, truncus arteriosus, and a right-sided aortic arch. The occasional inconstancy of these and the other anomalies should be borne in mind, however, and definitive diagnostic studies, such as cardiac catheterization, should be carried out before surgical intervention. Evidence of impaired pulmonary blood flow occurred in 19 of the 27 cases collected from the literature; pulmonary atresia was present in 11 cases and pulmonary stenosis in 7. Consideration of a shunt operation to increase pulmonary blood flow may be entertained in the management of these cyanotic infants, but a diagnosis of agenesis of the spleen by hematological means coupled with a foreknowledge of the high constancy of the associated anomalies should lead to a more definitive approach and estimate of prognosis. In 20 of the 27 collected cases the patients died before they reached the age of one year.

Ebstein's Malformation: A Clinical and Laboratory Study. R. A. Kilby, J. W. DuShane, E. H. Wood and H. B. Burchell. Medicine 35:161-183 (Sept.) 1956 [Baltimore].

The authors describe nine cases of Ebstein's cardiac malformation in three men between the ages of 26 and 35 years, three boys between the ages of 7 months and 11 years, and three girls between the ages of 10 and 13 years who were admitted to the Mayo Clinic. Cyanosis was evident at birth or early in childhood and persisted in five patients. In one of two patients in whom cyanosis had been noted at birth, the sign disappeared permanently; it reappeared in the other at 8 years of age. In one patient, acral cyanosis had been noted after exertion or exposure to cold since the age of 5 years. Cardiac catherization was performed in all nine patients. Every patient had a right-to-left shunt at an atrial level, although minimal arterial desaturation was present in three patients. Five patients were thought to have peculiar, distally displaced but competent tricuspid valves. In two patients, tricuspid insufficiency was considered to be revealed by the presence of ventricular pressure pulses in the true right atrium. No gross abnormality in the position of a competent tricuspid valve could be shown in two patients. Somewhat increased atrial pressures were obtained in these two patients and the impression of an anomalous arrangement of the bicuspid leaflet was gained in one of them. Five of the patients are living and four died. Four patients underwent cardiac operations in an attempt to relieve the right-to-left shunt and to prevent the possible occurrence of cerebral abscesses and paradoxic emboli. One patient has been greatly improved and at present is working part time. The three others died, one during the induction of anesthesia and two during the immediate postoperative period. One patient died of cardiac failure two years after the initial examination. Autopsy in two patients revealed no obvious cause of death besides Ebstein's cardiac malformation in one in whom the diagnosis thus was confirmed; cerebral infarction was found in the other.

Seventy-one additional cases of Ebstein's cardiac malformation were collected from the literature. The findings in the 80 patients with this malformation indicate that considerable variation occurs in this pathological aberration with respect to its effect or function. Attention is drawn to the unusual course that the blood may follow in some patients, if it is to fill the right ventricular chamber. It is theorized that in some patients such filling may be prevented because the valve is pushed against the free wall of the right ventricle by blood in the atrial portion of the right ventricle. Most cases of Ebstein's disease are associated with a typical clinical picture. This picture is complete if the electrocardiogram shows a tracing characterized mainly by the pattern simulating right bundle-branch block, although the R wave from the right precordium is of low voltage and of a multiphasic type. Auscultation reveals a double murmur in the left parasternal region, perhaps with a loud third heart sound, and the roentgenogram shows moderate cardiac enlargement with decreased pulmonary vascular markings. The phonocardiogram may be sufficiently characteristic to be of diagnostic importance.

An Association Between Blood Group A and Pernicious Anaemia: A Collective Series from a Number of Centres. I. Aird, H. H. Bentall, J. Bingham and others. Brit. M. J. 2:723-724 (Sept. 29) 1956 [London, England].

For several years studies on pernicious anemia were carried out in various hospitals in London, Oxford, Cambridge, Sheffield, Newcastle, and Glasgow, and the ABO blood groups of the patients were determined. The composite total number of 1,114 patients with pernicious anemia included 490 who were of group O, 503 of group A, 86 of group B, and 35 of group AB. The combination of data from these hospitals has shown with fairly high significance that pernicious anemia is commoner in persons of group A than in persons of group O, and also perhaps, though the numbers are small, than in persons of group B. The greater incidence in group A appeared in both sexes.

ABO Blood Groups and Secretor Character in Duodenal Ulcer: Population and Sibship Studies. C. A. Clarke, J. W. Edwards, D. R. W. Haddock and others. Brit. M. J. 2:725-731 (Sept. 29) 1956 [London, England].

Two hundred ninety-three patients with duodenal ulcer and their sibships were studied in an attempt to ascertain whether there is an association between blood group O and duodenal ulcer as has been suggested by recent reports from several areas of Europe and the United States. The findings in these previous reports were obtained by comparing the blood groups of ulcer patients with those in a control series of persons without ulcer in the same area. Such controls can be unsatisfactory, in that a population of mixed origin may contain elements with a high incidence both of group O and of duodenal ulcer without the two being causally connected. For this reason the authors had unaffected sibs among the studied sibships act as controls who were not subject to this criticism.

The data obtained from the 293 duodenal ulcer sibships gave no evidence to support the hypothesis that a person belonging to group O is more likely to have a duodenal ulcer than are his group A, B, or AB sibs. This result could be regarded as evidence in support of the suggestion that the previously reported association between blood O group and duodenal ulcer was due to racial stratification within the populations concerned. There are, however, considerable objections to this explanation, and a second hypothesis that would explain the previously reported findings suggests that it is not the blood group of the person that increases the likelihood of ulceration but, at least in part, the blood group of the person's mother. The children of group O mothers will have a higher frequency of blood group O than that found in the general population, and, if a group O mother did predispose her children to ulcer irrespective of their blood groups, both affected and unaffected offspring would have the same high group O frequency. The numbers in the authors' study, however, were far too small for any definite conclusions that would have confirmed this hypothesis.

The ability to secrete ABO blood group antigens in body fluids is an inherited characteristic, and it seemed possible that secretors and nonsecretors might have different susceptibilities to duodenal ulcer. The secretor character in the saliva of 514 unrelated patients with duodenal ulcer was therefore studied and the results were compared with those of 491 controls from the general population. There was a significantly higher proportion of nonsecretors in the patients with duodenal ulcer (35%) than in the controls (24.2%). This difference was found in both males and females belonging to each of the ABO blood groups and in both macroscopically and radiologically diagnosed cases. These data suggest that in nonsecretor persons duodenal ulcer may be about 45% more likely to develop than in secretors. For the same reason as in the association between group O and duodenal ulcer, the secretor characteristic was tested in the sibships of 262 patients with duodenal ulcer, and the results in the 262 families suggested that the relationship between nonsecretion and duodenal ulcer may hold within families. The possibility that the ABO and Lewis antigens may confer some protection against duodenal ulcer by virtue of their mucoid character has been discussed.

Incidence of the Common Forms of Human Leukemia. B. MacMahon and D. Clark. Blood 11:871-881 (Oct.) 1956 [New York].

In an attempt to assemble data on all residents of the borough of Brooklyn in whom a diagnosis of leukemia was made in the period from 1943 to 1952, a total of 1,792 abstracts of hospital records and 1,830 death certificates were obtained that gave information on 1,709 patients. The mean population of Brooklyn over the same period was used to express incidences of the various forms of leukemia in relation to color, sex, and age.

The incidence of leukemia in white males and females was 71.3 and 57.7 per million per year respectively. Corresponding rates for Negroes were 46.5 and 30.6. The white-Negro difference was decreased but not eliminated by standardization to allow for differences in the age distributions of the two populations. Sex ratios were lower for the acute forms of the disease than for the chronic forms, and, in both acute and chronic forms, for myeloid than for lymphatic cell types. No relationship of sex ratio to age at the time of the diagnosis or the initial white blood cell count was found. Each pathological variety of leukemia has its own distinct age incidence curve. The lymphatic forms appear to be more sharply associated with both extremes of age than do the myeloid varieties. That is, acute lymphocytic leukemia appears at a younger age than does acute granulocytic leukemia and the chronic lymphocytic form appears at an older average age than the chronic granulocytic variety.

The Present Status of the Diagnosis and Treatment of Syphilis. J. E. Vandow and N. Sobel. New York J. Med. 56:2796-2802 (Sept. 15) 1956 [New York].

The diagnosis of syphilis has become increasingly difficult because of the frequency of biologic false-positive serologic reactions. Considerable progress is being made toward solving this problem as a result of the recent development of a number of new laboratory tests. Four new serologic procedures and their application to the diagnosis of syphilis are discussed. These are the Treponema pallidum immobilization, immune-adherence, agglutination, and complement-fixation tests. These new tests are additional diagnostic aids in special situations but have not replaced the standard serologic test for routine use. In a study of 191 patients with positive blood tests suspected to be biologic false-positive reactions, the immobilization test was reactive in 66 (34.6%), indicating that syphilis was actually the cause of the positive serologic test in one-third of the cases. The clinical impression of a biologic false-positive reaction was confirmed in the remaining 125 patients. In patients in whom the diagnosis of latent syphilis was suggested by clinical data, this was verified in only half the patients. The schedules of treatment with penicillin and other antibiotics used by the New York City Health Department are described.

Obesity and Diabetes Mellitus. R. Murphy. J. Michigan M. Soc. 55:1209-1210 (Oct.) 1956 [St. Paul].

The obese diabetic patient differs in many respects from the thin diabetic patient. Most obese diabetic persons are adult. The onset of the disease usually occurs after the age of 40 years and the patients are predominantly women. Diabetes in the obese patient is usually stable in type. Often it can be controlled by reduction of dietary carbohydrates and the control maintained by reduction in weight. Ketosis rarely occurs, and, in those who require insulin, hypoglycemic episodes are not common. The apparent toleration of hyperglycemia has led to the mistaken idea that diabetes in the obese patient is "mild" and need not be given as serious consideration as diabetes in the thin individual. Actually, the obese diabetic patient is heir to all the serious complications, but usually there is not an absolute deficiency of insulin.

The antidiabetic sulfonamide drug carbutamide seems to be most effective in diabetic patients who still possess the capacity to secrete insulin, that is, in the obese group. The response to antidiabetic sulfonamides can be determined by estimating the blood sugar level before and four to six hours after a test dose of 2.5 or 3 gm. If the patient responds to the medicament by a significant fall in blood sugar, then a trial of treatment may be given, using 2.5 gm. on the first day, 1.5 gm. on the second day, and 1 gm. daily thereafter. If carbutamide is used, it is essential to remember the following points: 1. The medicament is an adjunct to, not a substitute for, dietary management. 2. The patient must be kept under close observation for the development of toxic side-effects, such as rash, leukopenia, crystalluria, and possibly jaundice. 3. Insulin must be used in the presence of infection, surgical operations, and especially with ketosis. 4. The antidiabetic sulfonamides are not an easy way out in the treatment of diabetes; they should be used with caution and only in patients who have proved that they are dependable.

SURGERY

Results of Mitral Commissurotomy for Mitral Stenosis: An Analysis of 48 Patients Followed from One to Five Years. J. L. Lee Jr., R. R. Shaw and D. L. Paulson. Texas J. Med. 52:729-734 (Oct.) 1956 [Austin, Texas].

Of 48 patients with mitral stenosis followed for from one to five years after mitral commissurotomy, 47 were in class 3 or class 4 before operation, or in terms of symptoms they were progressively incapacitated or were in congestive failure. There was one operative death and eight late deaths due to progressive heart disease. Of the patients who survived, 36 either had excellent results or were definitely improved, whereas 2 were not improved. Although these results are good and compare favorably with those reported in other larger series, the author feels that, through the use of newer diagnostic measures, chiefly cardiac catheterization of the right and left side, it will be possible to improve the results by eliminating from the operative group cases that are not suitable for operation.

Aneurysm of Thoracoabdominal Aorta Involving the Celiac, Superior Mesenteric, and Renal Arteries: Report of Four Cases Treated by Resection and Homograft Replacement. M. E. DeBakey, O. Creech Jr. and G. C. Morris Jr. Ann. Surg. 144:549-573 (Oct.) 1956 [Philadelphia].

DeBakey and associates report observations on four patients with extensive thoracoabdominal aneurysm of the aorta treated by resection and homograft replacement. In all of these patients the aneurysm extended from the lower descending thoracic aorta to the lower abdominal aorta and involved the celiac, superior mesenteric, and one or both renal arteries. The operative procedure consisted in excision of the aneurysm and replacement with an aortic homograft with restoration of continuity to the celiac axis and superior mesenteric arteries in all as well as to both renal arteries in two, and to one of the renal arteries in the other two patients. The most important consideration in extirpation of aneurysms of this type arises from the potential ischemic damage to such vital organs as the kidneys, liver, and gastrointestinal tract as a consequence of temporary arrest of circulation during the procedure. Two methods are available to overcome this problem, namely hypothermia and the use of a temporary shunt to conduct blood around the occluded segment.

Hypothermia was used in the first patient, but he died of renal failure one week after the operation. The superior mesenteric and both renal arteries were occluded for 105 minutes and the celiac artery for 120 minutes. Temporary shunts were employed in the other three patients. The successful results obtained in these patients emphasize the importance of performing the procedure in such a manner as to minimize the period of ischemia to the vital structures. The period of occlusion of the renal arteries ranged from 15 to 46 minutes. Serial renal function studies in these patients revealed a characteristic pattern of depression of function, as reflected by increase in the blood urea nitrogen level and reduction in renal blood flow and glomerular filtration rate during the first 4 or 5 days after operation with progressive return to normal during the subsequent 10 days to two weeks. The period of occlusion of the celiac artery in these cases ranged from 44 to 116 minutes. Studies of hepatic function revealed no significant alterations. The period of arrest of circulation through the superior mesenteric artery varied from 36 to 102 minutes, and no significant disturbances in gastrointestinal function were observed.

Cystic Medial Necrosis as a Cause of Localized Aortic Aneurysms Amenable to Surgical Treatment. H. T. Bahnson and A. R. Nelson. Ann. Surg. 144:519-528 (Oct.) 1956 [Philadelphia].

A patient with cystic medionecrosis of the aorta was a 39-year-old Negro male with a progressively enlarging fusiform aneurysm of the ascending aorta, who had been followed over an eight-year period. Chronic congestive heart failure occurred that appeared to be rapidly and irreversibly progressive. In the absence of syphilis and infection a diagnosis of cystic medionecrosis was made, and this was confirmed by examination of the surgical specimen. Approximately half the aneurysm of the ascending aorta was excised and the remaining vessel wrapped with a nylon binder. Slight constriction of the first portion of the aorta apparently relieved the previously incapacitating aortic insufficiency. Initially improved, he died suddenly five months later, his death being attributed to a myocardial infarction, although the visible infarct was a healing one. In the past year the authors have seen three additional patients with similar involvement of the ascending aorta and one of the distal aortic arch, all with histological evidence of cystic medionecrosis. This pathological condition, called Erdheim's cystic medionecrosis, has been previously recognized as a cause of aortic weakness and has been demonstrated in four groups of patients: 1. It is often present in cases of dissecting aneurysm and is thought to be the principal cause of dissection in young individuals. 2. It is commonly described as the cause of aortic weakness in cases of spontaneous rupture of the aorta. 3. It is one of the characteristic features of Marfan's syndrome (with, in addition, arachnodactyly, dislocated lenses, and a generalized defect in ground substance). 4. It is sometimes seen in slight degree in otherwise normal aortas.

The authors emphasize the production of localized aneurysms by cystic medial necrosis. Such aneurysms have been seen principally in middle-aged patients in the ascending aorta but also at the distal end of the aortic arch. In the latter location the lesion may be treated by excision and aortic anastomosis, possibly with an interposed graft. When the ascending aorta is involved the aortic valve may become incompetent as a result of dilatation of the valve ring. The aneurysm as well as the valvular incompetence have been relieved by excision of part of the circumference of the aorta and restoration of an essentially normal diameter. The structurally weakened aortic wall was reinforced with a nylon binder. The condition can be recognized clinically and should be treated before great dilatation of the aorta, aortic dissection, or chronic heart failure occur.

The Surgical Management of Achalasia of the Esophagus. H. R. Hawthorne, A. S. Frobese and P. Nemir Jr. Ann. Surg. 144:653-669 (Oct.) 1956 [Philadelphia].

The authors review observations on 35 patients with achalasia of the esophagus who were treated by a modified Heller operation, an extramucosal esophagocardiomyotomy. Follow-up studies including roentgen examinations and manometric studies of esophageal motility revealed that an excellent result was obtained in four-fifths of the group. Recurrent dysphagia, appearance of substernal pain, or gastrointestinal bleeding occurred in 21%. Regurgitation of gastric contents into the esophagus was demonstrated in each patient in whom the surgical result was unsatisfactory. The addition of pyloromyotomy failed to protect these patients from regurgitant esophagitis. The presence of esophagitis preoperatively or the presence of duodenal ulcer disease appears to affect the result adversely. The physiological basis for the good results is not clear. It seems that benefit is obtained by breaking the "circus movement" and eliminating spasm at the distal end of the esophagus rather than by any change in the esophageal motility.

Adrenalectomy for Control of Cancer of the Breast. M. H. Rabwin, D. H. Rosenblum, B. Simkin and others. California Med. 85:213-219 (Oct.) 1956 [San Francisco].

Combined oophorectomy and adrenalectomy was performed in 10 patients with metastatic carcinoma of the breast. All had metastasis to soft tissue and/or bone associated with active progressive symptoms due to the metastatic lesions. The metastatic lesions could be objectively demonstrated in every case. There was no selection as to age, pathological type of tumor, type of metastasis, or previous therapy. Eight of the 10 patients had had varying amounts of hormonal and x-ray therapy previously, despite which the disease was still progressing. Particular attention was given to the preoperative and postoperative management. In addition to the routine preoperative tests, serum electrolytes, calcium metabolism, and hormonal production were investigated, and a roentgenologic search for metastases was made. Preoperative preparation with cortisone given intramuscularly was frequently sufficient to carry the patient through the surgical procedures without incident or need of further steroid therapy.

In all but one of the patients the operation was done in two stages, bilateral oophorectomy and left adrenalectomy in the first stage and right adrenalectomy a week or 10 days later. In one instance the entire procedure was done in one stage. When the patient is in reasonably good condition, the one-stage procedure can be done safely. There were no surgical deaths. After the operation all of the patients were satisfactorily maintained by the oral administration of 50 mg. of cortisone daily in divided doses. Desoxycorticosterone was given sublingually in doses of 2 mg. daily. Remissions were achieved in 3 of the 10 patients; the other 7 died of metastatic disease. Cerebral or hepatic metastasis contraindicates adrenalectomy for metastatic cancer of the breast. Five of the seven patients not benefited by the operation had either cerebral or hepatic metastasis. The best candidates for adrenalectomy are premenopausal women who have previously had a clinical remission after oophorectomy and who have subsequently relapsed. The indications for adrenalectomy in the postmenopausal woman are not clear.

Needle Biopsy of the Parietal Pleura. P. Heller, W. F. Kellow and B. Chomet. New England J. Med. 255:684-690 (Oct. 11) 1956 [Boston].

The authors describe needle biopsy of the parietal pleura, which they carried out in 20 patients. The site of the biopsy is selected fluoroscopically. The skin is prepared for pleural aspiration. A no. 22 anesthesia needle is used for measurement of the thickness of the chest wall and the parietal pleura, this needle being slowly introduced until fluid is aspirated. After the anesthesia needle is withdrawn a Vim-Silverman needle is inserted a shorter distance, leaving room for protrusion of the split needle after the obturator has been removed. The split needle is advanced and is rapidly rotated in a manner similar to the technique of liver biopsy, and then the entire unit is speedily withdrawn. The specimen is usually small, often measuring about 3 mm., and may include intercostal muscle. Only one of the specimens thus far has included pulmonary tissue, and in this case there was no evidence of an adverse effect to the patient. The only complication of 22 needle biopsies in 20 patients has been a small hemothorax in one. This was recognized by an increase in the pleural effusion after biopsy and did not cause any serious consequence. A chest roentgenogram should be obtained 24 hours after biopsy.

The histological diagnosis was caseating granuloma in five cases, malignant neoplasm in four, and nonspecific fibrosis in nine; in 2 an insufficient specimen was obtained. Analysis of the five patients in whom a caseating granuloma was found demonstrates the common clinical problem with which a physician is often faced when he has only the traditional methods of examination available. The diagnosis of tuberculosis was suspected in only three of these patients before the biopsy, and neoplastic disease appeared to be more likely in the other two. The tuberculin test was positive in all five patients, whereas the histoplasmin, coccidioidin, and blastomycin tests were negative. Culture of the pleural fluid in three of these five patients remained negative, and in the other two patients the cultures were positive, but not until several weeks after the biopsy results had been obtained. Case reports demonstrate the usefulness of this procedure in patients with tuberculous pleural effusion. Needle biopsy of the parietal pleura may contribute significantly to the early detection of the cause of a pleural effusion. Although the specimens obtained were subjected only to histological examination, they should also be suitable for bacteriological studies.

Pleural Biopsy. I. A. Breckler, M. C. Hoffman, H. E. Hill and others. New England J. Med. 255:690-694 (Oct. 11) 1956 [Boston].

The Pulmonary Disease Center with which the authors are connected serves as a diagnostic center for chest problems in Air Force personnel. They subjected 16 patients with pleural effusion or blunted costophrenic angle to open pleural biopsy, which does not necessitate rib resection. The first five patients with pleural effusion were examined by needle and open biopsy techniques under local anesthesia. The open biopsy was no more difficult, and tissue specimens obtained were so superior that the needle biopsy method was abandoned. The pleura is approached through an intercostal incision, which is carried through intercostal muscles and endothoracic fascia to the pleura. The pleura is cleaned by blunt dissection and the visible portion grasped with an Allis forceps and excised. Experience taught that the most consistent and easily accessible point where the parietal and visceral pleura are fused is through the seventh or eighth interspace in an anterolateral position on the involved side. In most cases fusion in this area occurs as early as six weeks from the onset of the effusion, but a free pleural space does not contraindicate the biopsy even though a pneumothorax may result. Immediate catheter suction is instituted, and the patient is usually not even aware that his lung has collapsed. There were no other complications.

A portion of the fresh specimen was taken for bacteriological study, and the remaining tissue was fixed and stained. In 9 of 10 patients in whom tuberculous pleural effusion was suspected the diagnosis was confirmed by the finding in the specimen of typical histological evidence of tuberculosis. Acid-fast bacilli were demonstrated in five of the nine specimens. The 10th patient had a normal pleura on biopsy after four months of antituberculous chemotherapy; cavitation of the left lung, with a positive sputum, developed six months later. In this case the previously blunted costophrenic angle had disappeared, leaving a sharp angle at the time of biopsy. These 10 patients all had positive tuberculin reactions. In two patients with intrathoracic neoplasm a diagnosis was made or substantiated by pleural biopsy when other diagnostic techniques had failed. In two patients with streptococcic pneumonia with effusion, one patient with a residual hemothorax, and one patient with collagen disease, the pleural biopsy showed no specific changes.

The Surgical Significance of Ulcerative Colitis in Infants and Children. I. A. Meeker Jr. and P. Goff. West. J. Surg. 64:545-551 (Oct.) 1956 [Portland, Ore.].

Twenty-five infants and children with intermittent or chronic unremitting ulcerative colitis were admitted to the Children's Hospital, Los Angeles, between 1945 and 1955. The onset of the disease in most of the patients occurred at the time of some major emotional disturbance and was precipitated by separation or divorce of the parents, death of a close relative, environmental changes such as scout camp, summer camp, or relocation of the home, and extreme anxiety and concern over pubertal sex problems, such as masturbation. Chronic or recurring diarrhea and cramp-like abdominal pain caused weight loss, dehydration, and anemia, which made hospitalization necessary. The entire abdomen was rather tender and sensitive to palpation during the acute phase of the disease, and hyperactive intestinal sounds were frequently heard by auscultation. After control of the acute illness by medical measures, a proctoscopic examination was carried out with the aid of general anesthesia. The mucous membrane often appeared granular and grey and bled easily when touched, but an obvious ulcer crater was found only rarely. A considerable amount of mucus or mucopurulent exudate was noted occasionally in the rectal ampulla. Characteristic changes in the colon were revealed by roentgenologic examination in patients in whom the disease process had persisted for a prolonged period; there was loss of haustrations, and the colon had become foreshortened and tubular with loss of the redundant sigmoid loops; ulcerations were outlined by the barium column.

Two boys and six girls had a relatively mild form of the disease with two or three attacks of intermittent ulcerative colitis, but between these exacerbations they have had normally formed stools. The average age of these patients at the onset of the disease was 7 years. They were followed closely and were given continuous pediatric and psychiatric care with very gratifying results. None of these children was operated on and none went on to the more chronic unremitting form of the disease. The remaining 17 children, 8 girls and 9 boys, had the chronic unremitting form of ulcerative colitis. The average age of these patients at the onset of the disease was 8.8 years and the average duration of the disease was 5.4 years. All had either liquid or semisolid stools. Thirteen have been sustained successfully to date by medical management including administration of antibiotics to control infection, liberal use of whole blood transfusions to combat anemia and hemorrhage, and, in case of failure of these measures, judicious use of corticotropin or cortisone in doses appropriate to the age of the patient. Of the remaining four patients, one boy with the onset of his disease at 10 years of age who had ileostomy alone performed six years later died of carcinoma of the colon at the age of 21, after an interval of almost 11 years. The other three children have permanent ileostomies and have had total colectomy and abdominoperineal resection of the rectum, carried out in one stage in two of the patients. Each of these three children had irreversible x-ray changes in the colon, systemic manifestations of arthralgia, subcutaneous abscesses, and rectal fistula formation necessitating radical surgical intervention. All three are alive and well, have gained weight, and have been able to pursue far more normal healthy lives than was possible before surgery. Emergency ileostomy was rarely necessary, and more radical surgical procedure could be performed to cure patients with long-standing disease. Only those patients who have had their disease for more than 10 years without remission should be urged to undergo definitive surgery regardless of any psychogenic considerations.

Total Colectomy and Abdominoperineal Resection (Pan-Colectomy) in One Stage. M. M. Ravitch. Ann. Surg. 144:758-767 (Oct.) 1956 [Philadelphia].

In the Baltimore City Hospitals and the Johns Hopkins University Hospital pancolectomy (one-stage total colectomy and abdominoperineal resection of the rectum) is the preferred procedure for patients requiring operation for ulcerative colitis. Patients with polypoid adenomatosis of the colon are not denied operation because of advanced age or overriding additional disease. The indications for total colectomy and abdominoperineal resection are given. Anal ileostomy should be added in all cases of colectomy for polyposis and in suitable instances of colectomy for ulcerative colitis. The less profoundly ill patients will tolerate the entire one-stage procedure without difficulty and will be spared the risk of additional anesthesia, incision, and operative procedure. The more profoundly ill will derive sufficient benefit from the ablation of the diseased intestine to compensate for the moderate increase in magnitude of the operative procedure and will be spared the dangers of sepsis or hemorrhage attendant upon retention of the diseased rectum in ulcerative colitis.

The Use of Cortisone in Acute Diffuse Peritonitis. N. Molino and G. B. Xiume. Minerva med. 47:1993-1995 (June 23) 1956 (In Italian) [Turin, Italy].

Four patients operated on for severe acute diffuse peritonitis were treated with a combination of antibiotics and cortisone. Marked and speedy improvement in their general condition followed. The postoperative course of the disease was shortened and complete recovery followed. Deficiencies in the sodium and potassium metabolism and excretion did not occur in any of the patients. Cortisone had a marked antistress effect.

GYNECOLOGY & OBSTETRICS

Some Clinical Aspects of Factitial Proctitis. B. J. Kaplan. Connecticut M. J. 20:357-363 (May) 1956 [New Haven, Conn.].

Factitial proctitis occurred in 62 (38.36%) of 159 women between the ages of 20 and 78 years with gynecologic pelvic malignancy, for which they received irradiation therapy. One hundred forty-four (90.57%) of the 159 patients had carcinoma of the cervix and 15 had other pelvic malignancies. All patients with factitial proctitis had carcinoma of the cervix. One hundred nine patients were followed from the onset of the irradiation therapy for periods up to 21 months. The irradiation therapy consisted of deep x-ray therapy and administration of radioactive cobalt, followed by intracavitary radium application. Symptoms of factitial proctitis occurred in 43 of the 62 patients within a period of from three weeks to five or seven years after the initial irradiation therapy. Nineteen patients (30.65%) had no symptoms, although objective findings were present in the rectum or lower sigmoid. Symptoms consisted of bleeding, diarrhea, pain, constipation, abdominal cramps, rectal tenesmus, and excessive mucoid discharge. Proctoscopic examination revealed that telangectasia was present in all grades of proctitis. The earliest changes appeared as a mild or moderate erythema with some edema of the mucosa. The severity of the process may progress and lead to inflammation and eventually to ulceration of the intestine, usually on the midanterior rectal wall. An ulcer will occasionally continue to penetrate through the anterior rectal wall until a rectovaginal fistula results. Often it is impossible to tell whether one is dealing with infiltrating carcinoma or inflammatory tissue. Repeated proctoscopic examinations should be performed in all patients having undergone pelvic irradiation.

The 62 patients (82.86%) had mild proctitis and were treated topically with hydrocortisone. The course of therapy in most patients consisted of eight consecutive weeks of two daily rectal applications of 75 mg. of 2.5% hydrocortisone acetate. In some patients treatment was continued for 12 weeks. A pronounced proctoscopic improvement was noted after two or four weeks of treatment. Untreated lesions may heal within a period of from 12 to 24 months. Healing time was shortened by the treatment to three or four months. There is a definite possibility of intestinal perforation with topical application of hydrocortisone, and this possibility should be kept in mind. No other untoward reactions were observed.

Chronic Hypertension Following Pre-Eclamptic Toxemia: The Influence of Familial Hypertension on Its Causation. F. J. Browne and D. R. Sheumack. J. Obst. & Gynaec. Brit. Emp. 63:677-679 (Oct.) 1956 [London, England].

As a result of examining the blood pressures of parents and siblings of 100 primiparas who had preeclamptic toxemia and were followed up in the postnatal clinic, there seems to be sufficient evidence to suggest that those who belong to hypertensive families run a certain risk of developing residual hypertension immediately after the pregnancy in question. The evidence suggests that if the patient with preeclamptic toxemia does not belong to a hypertensive family, residual hypertension will not develop. It is probable that in patients in whom chronic hypertension develops the preeclamptic toxemia does not cause the hypertension but simply unmasks a familial tendency to hypertension and makes it develop earlier than it would otherwise have done.

Black Urine ("Black Water") After Use of Quinine During Pregnancy. U. Brost. Geburtsh. u. Frauenh. 16:698-706 (Aug.) 1956 (In German) [Stuttgart, Germany].

The first of the two patients presented was a 33-year-old woman who was given quinine to induce labor, her pregnancy having progressed beyond term. Since the first doses of quinine failed to induce labor, treatment with quinine was repeated on the following day. Petechial points appeared on the tongue, the oral mucous membranes, and on various parts of the body. The urine obtained by catheterization was black and contained many erythrocytes and a few leukocytes. Examination of the blood disclosed a decided thrombopenia, a prolonged coagulation time, and a decrease in the osmotic resistance of the erythrocytes. Fortunately, delivery did not start until after the hemorrhagic tendency had been corrected by large doses of vitamins C and K. Delivery was uneventful despite continued microhematuria. Subsequent inquiry revealed that a few weeks before the woman was hospitalized for the induction of labor she had taken a cold remedy known to contain quinine. She recalled that after that she developed "large blue spots" after only slight bruising. Some months later the woman reported that a sister of hers likewise had developed skin hemorrhages after taking a quinine preparation. The author deduced from this that a familial idiosyncrasy to quinine played a part in the development of the severe hemorrhagic reaction to quinine.

The second patient was an unmarried woman, aged 21, who took large doses (9 gm.) of a quinine preparation over a period of three days in order to induce an abortion. Here again the urine was black, and when the blood was examined the supernatant serum was red. Renal insufficiency developed, and the patient died from uremia and cardiovascular failure. The therapy of the quinine-induced hemoglobinuria should aim at restoring normal blood coagulation and at counteracting the increased permeability of the vascular walls.

Post-Eclamptic Vegetablism. C. W. F. Burnett. J. Obst. & Gynaec. Brit. Emp. 63:680-685 (Oct.) 1956 [London, England].

Burnett describes observations on a 26-year-old multipara in whom severe eclampsia progressed to a vegetative state that terminated in death after six weeks. Although patients with post-eclamptic psychosis and aphasia have been frequently described, only two similar cases of a vegetative existence following severe eclampsia appear in the literature. One of these two women died after six years of a vegetative existence and the other three months after delivery. The histological features of the brains are compared. The hypertension and prolonged anoxia that occur with severe eclampsia give rise to a hypertensive encephalopathy of profound degree, which, if the patient survives, produces areas of ischemic necrosis in both the grey and white matter that destroy the higher cerebral centers. In consequence of this damage the patient is reduced to a vegetative form of existence, from which there is no recovery. Such cases were rare in the past, as the severity of the eclamptic process necessary to produce such a severe encephalopathy usually killed the patient. With the improved treatment of eclampsia by means of hypotensive drugs and the salvage of patients who would have otherwise died, it may be expected that they will be encountered more frequently in the future. It is to be hoped that this threatened increase will be cancelled by a decreased incidence of eclampsia itself, for it is no therapeutic achievement to save the life of a patient at the cost of her living a decerebrate existence.

Bacteremia as a Cause of Obstetric Shock. J. G. Dumoulin and G. R. Steed. J. Obst. & Gynaec. Brit. Emp. 63:739-742 (Oct.) 1956 [London, England].

The histories of two women are cited to illustrate that severe obstetric shock can result from bacteremia acquired during labor. In both patients blood culture yielded Bacterium coli. The infection was acquired in the first patient during surgical induction of labor and in the second as the result of an infected blood transfusion. Both patients recovered. In view of the satisfactory response to vigorous treatment, this rare but dangerous condition should be borne in mind in cases of unexplained shock.

Analysis of Amniotic Fluid Cells for Diagnosis of Foetal Sex. L. Sachs, D. M. Serr and M. Danon. Brit. M. J. 2:795-798 (Oct. 6) 1956 [London, England].

An analysis of amniotic fluid cells was made in an attempt to diagnose the fetal sex in 40 cases in the ninth month and in 8 cases in the third, sixth, and seventh months of pregnancy. Amniotic fluid was obtained before delivery by puncture of the membranes and in the earlier months of pregnancy by abdominal puncture, except for the patient in the third month, in whom the amniotic fluid was obtained in the course of hysterectomy. A clear sex difference was found when the diagnosis was based both on the percentage of cells with a karyosome and on the percentage of cells with a karyosome at the nuclear membrane. The latter determination is to be recommended as a routine procedure, since it is easier to carry out.

In the 47 cases in the sixth, seventh, and ninth months of pregnancy there was a mean of 4% of cells with a karyosome at the nuclear membrane in males and a mean of 35% of such cells in females. The karyosome was also larger when found in cells of a female than in cells of a male. Three main types of epithelial cells, namely, basal, precornified or cornified, and keratinized cells, were observed in the amniotic fluid. Of these, the basal and precornified cells proved to be most suitable for the diagnosis of sex.

Determinations of the percentage of cells in the amniotic fluid that are suitable for the diagnosis of sex gave a mean of 12% suitable cells for both males and females in the sixth, seventh, and ninth months of pregnancy. In the one case in which the amniotic fluid was obtained in the course of hysterectomy at the end of the third month, 61% of the cells were suitable for the diagnosis; the diagnosis of female sex on the amniotic fluid cells was confirmed by a study of embryonic membranes. It was also possible to make a diagnosis on the cells in the fluid of an 8-week-old aborted embryo, and this was again confirmed by a study of embryonic membranes.

PEDIATRICS

Observations on the Etiology of Acute Laryngotracheobronchitis, Toronto, 1953-1954. E. A. Morgan, J. A. Turner, A. J. Rhodes and others. Canad. M. A. J. 75:638-641 (Oct. 15) 1956 [Toronto, Canada].

Fifty-two boys and 18 girls between the ages of 6 months and 10 years with acute laryngotracheobronchitis were admitted to the Tracheitis Unit of the Hospital for Sick Children in Toronto, Canada, between 1953 and 1954. All of them had two or more of the following symptoms: coryza, hoarseness, croupy cough, stridor, and dyspnea. Bronchoscopy was performed on 21 children, 8 of whom had supraglottic edema, 5 generalized edema, and 8 subglottic edema. Micrococcus (Staphylococcus) pyogenes was isolated from 28 of the 70 patients. Streptococcus pneumoniae was isolated from 23 patients. Hemophilus influenzae, type B, was found in one patient with the typical clinical picture associated with this infection. These findings confirmed earlier reports that there is no constant pattern of organisms in these cases. Twenty-one patients required tracheotomy. Inoculation of tracheal secretions into tissue cultures revealed agents cytopathogenic for tissue cultures of human embryo lung and monkey kidney cells in five cases, but only two of these agents could be propagated serially. The changes produced in monkey kidney cells took about six or eight days to appear in the case of the two strains that were successfully propagated.

The clinical and bacterological findings in these patients agreed with the aspect of the disease as described by Neffson in his monograph on acute laryngotracheobronchitis. The recognition of the severe case with poor air entry but only a muffled stridor is vitally important because tracheotomy is lifesaving. The results of modern treatment with cool, moist air, antibiotics, and tracheotomy were gratifying; only one of the 70 patients died.

Cortisone Therapy of Lye Burns of the Esophagus. E. S. Ray and D. L. Morgan. J. Pediat. 49:394-397 (Oct.) 1956 [St. Louis].

Since 1954 the authors have used cortisone and antimicrobial drugs in 11 children with lye burns of the esophagus. In view of the danger of serious mediastinal and pulmonary complications from cortisone therapy, the children were hospitalized during the period of cortisone administration. The ages of the 11 children ranged from 1 to 4 years, and 7 had severe and 4 had mild burns. Treatment with cortisone was started within 24 hours after the burn in 10 of the children. One child did not enter the hospital until the fourth day after the ingestion of the lye, at which time complete esophageal obstruction was present. After 3 days of steroid therapy this patient was able to swallow liquids, and at the end of 10 days she was able to take a general diet and a barium swallow was normal. However, a stricture of the esophagus developed in this child three months later that has required bougienage. This experience is further evidence of the ineffectiveness of steroid therapy when administration is delayed.

The authors favor the administration of olive oil and milk at frequent intervals to these patients. Diet is limited to liquid foods for three days and then puréed foods during the first two weeks. After that the child is given a general diet. Antimicrobial drugs (either a combination of streptomycin and penicillin or one of the broad-spectrum antibiotics) are given to all patients. Since most of these children have dysphagia, the drugs are given parenterally. Cortisone in doses of 25 mg. is given every six or eight hours; initially, during the period of dysphagia, it is given intramuscularly, later orally. The duration of cortisone therapy ranged from 7 to 30 days, the optimal duration being indefinite. The 10 children who received cortisone promptly had no evidence of stricture and have remained on a general diet during the period of follow-up (6 to 28 months). No complications resulted from the cortisone therapy.

Reserpine in Cerebral Palsy. R. D. Harris and E. H. Rowley. J. Pediat. 49:398-400 (Oct.) 1956 [St. Louis].

Following a pilot study with reserpine in 27 children with cerebral palsy ranging in age from 2 to 12 years, the authors began a controlled evaluation in 42 patients with cerebral palsy (including the initial 27). The 42 were divided into two groups. Group 1 was given 0.25 mg. of reserpine (elixir Serpasil) daily. Group 2 was given placebos. Group 1 received reserpine for a two-week period, after which they were changed to placebos and group 2 was then given reserpine for a two-week period. The two groups were as nearly identical in diagnosis as possible. The nursing personnel reported that all children receiving reserpine were happier and more cooperative and that there were fewer emotional upsets. In many instances the tension was reduced so that the children were better able to cooperate in the physiotherapy program. In some children in whom there had been fear of falling when walking, this fear was allayed. They tolerated their braces better and were able to manage them with greater ease. Children who were usually restless at night slept better, and the usual dose of sedative was lowered or completely withdrawn. There was an increase in appetite, and many showed weight gains.

Four illustrative case histories are presented. No significant changes in blood pressure were observed, although there was a slight reduction in cardiac rate. "Snuffy nose" was observed in some instances. Urticaria in a 4-year-old child subsided when reserpine was withdrawn and did not recur when treatment was resumed with a smaller dose (0.1 instead of 0.2 mg. twice daily). Drowsiness was sometimes noted, particularly with the larger doses of the drug. Reserpine was a helpful adjunct in a training program for children with cerebral palsy. The drug induced better cooperation, replaced sedations, and served as a tranquilizer in emotional states. It was especially beneficial in allaying tension in tension athetosis and in reduction of tremor in tremor athetosis. Dosage must be individualized, but 5 minims (0.02 mg.) of Serpasil elixir daily is adequate for maintenance therapy in small (25 to 30 lb. [11.3 to 13.6 kg]) children.

Clinical Features of Aseptic Meningitis Caused by Coxsackie-B Virus. D. L. McLeon, A. J. Beale, G. A. McNaughton and A. J. Rhodes. Lancet 2:701-703 (Oct. 6) 1956 [London, England].

The clinical features of 17 children with aseptic meningitis due to Coxsackie-B virus are described. They formed part of a series of 96 cases of aseptic meningitis diagnosed as "nonparalytic poliomyelitis" and studied at the Hospital for Sick Children in Toronto, Canada, from 1950 to 1955. Most of these children were hospitalized shortly after an abrupt onset of symptoms indicating meningeal irritation. Most were followed after discharge, when convalescent serums were collected. On admission, or as soon as possible after, stools, blood, and cerebrospinal fluid were collected for virus studies. The techniques of examination for viruses included the inoculation of suckling mice, monkeys, and monkey-kidney monolayer tissue cultures by standard methods. All except one of the 17 children (ranging in age from 4 to 11 years) yielded a Coxsackie-B virus that could be assigned to one of Dalldorf's antigenic types. Three patients excreted the same antigenic type of virus in stools and cerebrospinal fluid. Ten of the 12 patients who provided suitable samples of serum showed during convalescence a rise in antibody to the homologous Coxsackie virus isolated from stools.

All 17 children were adequately studied to exclude concurrent infection with poliomyelitis. One of the objects of this study was the simplification of the differential diagnosis, but this was not achieved. It did not prove possible, in the indivdual case, to distinguish between aseptic meningitis caused by Coxsackie-B, poliomyelitis, or "orphan" viruses. A knowledge of the prevalent disease in the community may suggest the likely diagnosis, a case of aseptic meningitis being likely to be due to Coxsackie-B, poliomyelitis, or mumps virus if pleurodynia, paralytic poliomyelitis, or mumps is present in the community. Even during epidemics of paralytic poliomyelitis, however, there is evidence that some cases of aseptic meningitis are not due to polomyelitis. It seems that about 20% of cases of aseptic meningitis in Ontario are caused by Coxsackie-B virus.

THERAPEUTICS

The Effect of ACTH and Cortisone on Gastroduodenal Ulcer: Experimental Study. F. P. Tinozzi and G. Dozio. Minerva chir. 11:699-703 (Aug. 15) 1956 (In Italian) [Turin, Italy].

The authors studied the effect of adrenal hormones on gastroduodenal ulcer, or, more particularly, the way in which these hormones are related to the occurrence of hemorrhage in ulcerous lesions of the gastroduodenal tract. Fifty guinea pigs with an average weight of 400 gm. were put on a monophagic diet low in vitamins. This diet produced in the animals lesions similar to gastroduodenal ulcer in man. The animals were divided into 5 groups of 10 guinea pigs each. The first group was kept as a control; it was put on a monophagic diet and received no hormones. The second group was treated with 6 mg. of corticotropin (ACTH) per day, beginning when the monophagic diet was started. The third group was treated with 6 mg. of corticotropin per day beginning 15 days after the monophagic diet was started. The animals of the fourth group received 6 mg. of cortisone per day beginning when the monophagic diet was started. Animals of the fifth group received 6 mg. of cortisone per day beginning 15 days after the monophagic diet was started.

Some of the guinea pigs in the first group were killed after the 13th or 15th day. Gastroduodenitis with hemorrhage was found, especially in the juxtapyloric region. The rest of the group died after from 45 to 55 days. Hemorrhagic gastroenteritis was present in all and gastroduodenal ulcers in 85%. The animals of the second group died after from 40 to 50 days. All of them had gastroenteritis, but none had ulcers. The animals of the third group presented after death hemorrhagic gastroduodenitis with ulcers, and three had a juxtapyloric perforated ulcer. Treatment with cortisone had no effect on the animals of the fourth and fifth groups, in which the findings were the same as in the first group.

Corticotropin and cortisone have no real ulcerogenic effect. Cortisone has no effect on gastroduodenal ulcers caused by a monophagic diet or on the occurrence of complications such as hemorrhage and perforation. Corticotropin given before the occurrence of a gastroduodenal ulcer has an inhibiting effect. If it is given after ulcers have developed, corticotropin causes complications.

Pellagra Caused by Isoniazid. R. J. Harrison and M. Feiwel. Brit. M. J. 2:852-854 (Oct. 13) 1956 [London, England].

Pellagra occurred in a 45-year-old woman who was given 300 mg. of isoniazid daily combined with 20 mg. of pyridoxine hydrochloride three times daily for multiple sclerosis of 20 years' duration. The patient's appetite had always been poor, and her intake of food was inadequate. During a particularly sunny summer, she had burning sensation in the hands and feet, and typical symmetrical pellagrous dermatitis developed on the hands and feet. Isoniazid was withdrawn. Her symptoms persisted for the next three weeks. She continued to take the same inadequate diet. The burning sensations in hands and feet did not let her sleep at night with her extremities covered. The latter symptoms were rapidly relieved when the patient was given 1 gm. of nicotinamide daily. The dermatitis improved, and within 18 days the skin appeared normal.

As the symptoms of pellagra appeared in the course of isoniazid therapy, there seemed to be a cause-and-effect relationship. Other clinical observations were collected from the literature that pointed to isoniazid being a contributory factor in producing pellagra when the patient was in a prepellagrous condition. These clinical findings suggest a possible metabolic antagonism between isoniazid and nicotinamide. Isoniazid bears an undoubted structural similarity to nicotinamide, which is an integral component of an essential oxidation-reduction coenzyme, i. e., diphosphopyridine nucleotide. Experimental work has shown that it is possible by enzyme action to cause an exchange of isoniazid for the nicotinamide portion of diphosphopyridine nucleotide; this points to a mechanism by which isoniazid might produce nicotinamide deficiency, but in experiments on the whole animal this has not yet been shown. The biological antagonism between isoniazid and pyridoxal is caused by a purely chemical reaction. The suggestion that the pellagra-producing effect of isoniazid depends on the patient's initial level of nicotinamide being low would cover the facts observed in the patient. An apparent relationship between isoniazid and a condition that is caused specifically by a nicotinamide deficiency points to an interference by isoniazid in nicotinamide metabolism; as an integral component of diphosphopyridine nucleotide, nicotinamide has its most important known metabolic function. The question remains whether these observations are a reflection in man of the mechanism by which the tubercle bacillus is inhibited by isoniazid.

Modification of Abnormal Serum Lipid Patterns in Atherosclerosis by Administration of Sitosterol. M. M. Best and C. H. Duncan. Ann. Int. Med. 45:614-622 (Oct.) 1956 [Lancaster, Pa.].

Sitosterol was administered to 24 patients for sufficient periods of time to evaluate its effect on serum cholesterol and other lipids. Several types of sitosterol suspensions were employed in early studies, but during the last 18 months a 20% suspension of predominantly beta sitosterols has been used. Six to 8 gm. of sitosterol were administered orally immediately before the ingestion of food, the usual total per day being 18 to 25 gm. With this treatment the mean decrease in serum cholesterol was 15.5% of the control level. The absence of toxic effects permits further study of the possible therapeutic value of sitosterol in human atherosclerosis.

PATHOLOGY

Cancer and Atherosclerosis. A. Elkeles. Brit. J. Cancer 10:247-250 (June) 1956 [London].

The incidence of calcified atheroma was investigated in patients with cancer and in controls over the age of 50 years. Radiography of the abdominal aorta has proved to be a valuable method for recognizing calcified atheroma during life. The abdominal aorta was radiographed in 1,116 patients over 50 years of age, comprising 416 cases of cancer of various organs and 700 controls. A low incidence of calcified atheroma was found in the cancer patients (18.7%) compared with the controls (36.7%). This difference is even more pronounced in the 71 to 80 age group, 28.4% against 71.9%. Calcified atheroma is rare in patients with carcinoma of the stomach and its incidence is low in those with carcinoma of the prostate and breast. The percentage of calcified atheroma in patients with cancer of the respiratory tract, however, does not differ from that of the control series. The hypothesis is proposed that the incidence of calcified atheroma is low in patients with cancers that are influenced by genetic factors or are hormone dependent. The incidence of calcified atheroma in patients with cancers predominately caused by exogenous carcinogenic agents does not differ from the control series. Persons with marked atherosclerosis are less likely to develop cancer of certain organs, e. g., of the stomach, breast, and prostate.

Patchy Myocardial Necrosis in Rabbits After Shock Doses of Histamine and Peptone. B. M. Herbertson. J. Path. & Bact. 72:137-141 (July) 1956 [Edinburgh, Scotland].

The experiments described demonstrate that histamine and peptone shocks may cause myocardial lesions in the rabbit identical with those found after anaphylactic shock or severe pulmonary embolism. In a previous discussion it was considered that in both the latter conditions myocardial ischemia accompanying distension of the right ventricle and atrium was the fundamental cause of the injury. As the alterations in the dynamics of the cardiovascular system produced the injections of histamine and peptone are similar to those found after anaphylactic shock and pulmonary embolism, it is probable that the mechanism of the lesions is also essentially the same.

Anticoagulant Therapy of Acute Myocardial Infarction: An Evaluation from Autopsy Data with Special Reference to Myocardial Rupture and Thromboembolic Complications. K. T. Lee and R. M. O'Neal. Am. J. Med. 21:555-559 (Oct.) 1956 [New York].

The effects of anticoagulant therapy have been evaluated from clinical and autopsy data in 500 patients with acute myocardial infarction who were treated and who died at Barnes Hospital in St. Louis between 1910 and 1954. One hundred seventy-four patients with myocardial infarction were admitted to and died at this hospital before the advent of the anticoagulant drugs, and of the 326 patients who were admitted after the introduction of anticoagulant therapy 108 were treated with anticoagulants and 218 were not. Intravascular thrombi complicating acute myocardial infarction were observed at autopsy in a significantly greater percentage of patients who did not receive anticoagulants than in patients who received adequate anticoagulant therapy within three days of the clinical onset of the infarction. This difference was apparent only when patients who died within three days of the clinical onset of the infarction were omitted from the comparison. This omission was justified because a much greater proportion of untreated than treated patients died within the first three days after onset of the infarction and because thrombi were less common in patients who died early in the illness. The incidence of thrombi was not affected if initiation of anticoagulant therapy was delayed more than three days after the clinical onset of the infarction. This finding suggests that anticoagulant therapy is not effective unless begun within three days of the clinical onset of the infarction.

Myocardial rupture occurred five times as frequently among anticoagulant-treated patients as among untreated patients in the same period. However, no significant over-all increase in myocardial rupture occurred between 1910 and 1954. The possibility exists that selection of patients receiving anticoagulant therapy accounted for the high incidence of rupture in the anticoagulant-treated patients, but no support for this explanation was found in the clinical histories. The incidence of myocardial rupture in untreated patients decreased slightly in the years between 1910 and 1954.

Hemopericardium without myocardial rupture was not significantly more frequently observed in patients treated with anticoagulants, and in none of the cases was the amount of blood considered sufficient to have caused the patient's death.

Malignant Paraganglioma of the Organ of Zuckerkandl. W. A. Haug and H. W. Baker. A. M. A. Arch. Path. 62:335-339 (Oct.) 1956 [Chicago].

The authors describe a case of malignant paraganglioma arising from the organ of Zuckerkandl (extra-adrenal abdominal chromaffin tissue) in a 60-year-old man complaining of low back pain of five months' duration. The pain was constant, aggravated by walking or coughing, and accompanied by numbness and weakness of the left lower extremity. A poorly defined, firm, deeply situated mass, measuring 8 by 10 cm., was palpable just above the angle formed by the spine and the left iliac crest. An attempt was made to obtain a biopsy specimen of this left lumbar mass by a posterior approach. A vascular, yellow-gray tumor was discovered lying within the quadratus lumborum muscle and invading the spine. Upon incision into the tumor profuse hemorrhage occurred. The tissue removed at operation was reported by the department of pathology as adenocarcinoma, possibly metastatic from the kidney or adrenal gland. The patient died six months after the operation.

On autopsy a bulging, lobulated fusiform mass was found partially covered by and invading the psoas muscle. It was located retroperitoneally, in the left paravertebral region, immediately adjacent to the bifurcation of the aorta. On microscopic examination, a high-power view of the tumor revealed large polygonal and elongated epithelial-like cells. A medium-power view of the tumor showed a syncytial pattern with sparse stroma. Gomori's chromaffin tissue stain on formalin-fixed tissue revealed cytoplasmic granules with positive chromaffin reaction On section, the enlarged liver was seen to be literally replaced by metastatic tumor nodules measuring from 1 mm. to 8 cm in size. These metastatic lesions appeared virtually identical with the parent tumor except that the cytoplasm of some cells appeared basophilic.

The site of the primary neoplasm, just lateral to the bifurcation of the abdominal aorta, suggests that it originated in the organ of Zuckerkandl. This tumor is the third malignant paraganglioma reported to have arisen in this location. Assay for epinephrine was not performed on the tissue obtained at operation or at autopsy. At no time during the hospitalization of the patient was hypertension or any other evidence of sympathetic overactivity observed. Although the two malignant paragangliomas of the organ of Zuckerkandl previously reported were both functioning tumors, most of the malignant paragangliomas arising in other sites, including the adrenal medulla, have shown no evidence of physiological activity.

Mitral Stenosis and Pulmonary Arteriosclerosis: Correlation of Pulmonary Arteriosclerosis, Right Ventricular Hypertrophy, and Thromboembolism in Autopsied Patients Who Died with Mitral Stenosis. W. A. Thomas, K. T. Lee, E. R. Rabin and R. M O'Neal. A. M. A. Arch. Path. 62:257-261 (Oct.) 1956 [Chicago]

The relations between pulmonary arteriosclerosis, right ventricular hypertrophy, and pulmonary thromboembolism were studied by examining autopsy records and microsections of the lung from 86 patients with mitral stenosis as a principal anatomic diagnosis. Right ventricular hypertrophy was taken as presumptive evidence that pulmonary hypertension had been present during life. For comparison, a "normal" (control) group of 50 patients with neither cardiac nor chronic pulmonary disease was selected by age from recently performed autopsies.

Thirty-five (41%) of the 86 patients with mitral stenosis had "moderate" or "advanced" arteriosclerosis of their small muscular pulmonary arteries, and none of the patients in the control group had more than "slight" pulmonary arteriosclerosis. There was no significant correlation between the presence of moderate or advanced pulmonary arteriosclerosis and the presence of right ventricular hypertrophy. This finding suggests that pulmonary hypertension is not an important factor in the production of arteriosclerosis of the small pulmonary arteries in patients with mitral stenosis. Evidence of obvious thromboembolism consisting of clearly recognizable organized or fresh thrombi or infarcts in the lungs was observed in 26 (30%) of the patients with mitral stenosis. Moderate or advanced pulmonary arteriosclerosis was present in 18 (70%) of the 26 patients with thromboembolic phenomena, and only 17 (28%) of the 60 patients without demonstrable thromboembolic phenomena had moderate or advanced pulmonary arteriosclerosis. Correlation between the presence of moderate or advanced pulmonary arteriosclerosis of the small pulmonary arteries and the presence of thromboembolic phenomena in the lungs thus was highly significant, suggesting that pulmonary thromboembolism is an important factor in the pathogenesis of pulmonary arteriosclerosis.

Although this study was concerned primarily with factors associated with pulmonary arteriosclerosis, it also has physiological implications that may be useful in explaining the benefit derived from mitral commissurotomy. The absence of a significant correlation between the presence of moderate or advanced pulmonary arteriosclerosis and right ventricular hypertrophy suggests that the degree of pulmonary arteriosclerosis observed in most patients with mitral stenosis is in itself insufficient to cause a significant increase in the pulmonary vascular resistance.

The Laurence-Moon-Biedl Syndrome. C. F. Ross, L. Crome and D. Y. Mackenzie. J. Path. & Bact. 72:161-172 (July) 1956 [Edinburgh, Scotland].

Clinical and postmortem studies on a 23-year-old man with the classical features of the Laurence-Moon-Biedl syndrome are presented. Laurence and Moon in 1866 reported on four patients in one family presenting a syndrome of obesity, hypogenitalism, mental deficiency, and retinitis pigmentosa. Subsequent reports added polydactyly to these abnormalities. Three hundred cases of this syndrome have been reported up to 1955. Autopsy studies have been reported in only 10 of these, and most of them were incomplete, the eye, for instance, having been examined in only two cases. The main alterations in the brain of the authors' patient were lipofuscin-like pigment in all of the nerve cells, which were somewhat reduced in number, patchy gliosis and slight demyelination of the optic tracts, and chiasma. The hypothalamus was essentially normal. The endocrine glands, in particular the pituitary, were normal. The eyes showed the changes of primary pigmentary degeneration. The kidneys were the seat of acute or chronic pyelonephritis. Death resulted from uremia. Uremia has been a frequent cause of death in the Laurence-Moon-Biedl syndrome. The type of renal disease is not constant; glomerulonephritis appears to be the commonest, but vascular disease, pyelonephritis, and hydronephrosis have all been described. The finding of a persistent fetal structure by Griffiths may be important, since his is the youngest patient examined and there was no superimposed renal disease. It is known that persistence of fetal structures predisposes to inflammations, and it would appear that in the Laurence-Moon-Biedl syndrome there is some obscure renal inferiority.

The Pathogenesis of Atheroma of the Coronary Arteries. C. I. Levene. J. Path. & Bact. 72:83-86 (July) 1956 [Edinburgh, Scotland].

The coronary arteries were examined histologically in 98 hearts, from all age groups, in order to determine the sequence in which deposition of fat, calcium, necrotic debris, and fibrin and vascularity of intima and media occur. The study confirmed that fibrin was the cause of the progressively enlarging fibrous intimal plaques. Other changes appeared to result from the failure of the superficial and deep zones of organisation to link up. Mensuration confirmed that localised intimal thickening is associated with thinning of the underlying media.

Osteoperiosteal Lesions of the Leg in the Course of Chronic Phlebopathy of the Lower Extremity. C. Mairano and P. M. Pasquero. Minerva chir. 11:541-546 (June 30) 1956 (In Italian) [Turin, Italy].

The authors studied osteoperiosteal lesions of the leg in the course of chronic phlebopathy of the lower extremity in 40 patients with varicositis and 30 patients with phlebitis. Damage to the bone was present in most cases. Superficial capillary circulation with altered local metabolism is the main cause for osteoperiosteal damage. Infection plays a secondary role. The altered physiochemical character of the interstitial fluid has a chronic irritating effect on the bone and periosteal cells. Hyperfunction or hypofunction follow according to the intensity of the stimulus of these cells. Hyperostosis and bone thickening follow in case of hyperfunction, osteoporosis in case of hypofunction. The periosteum does not remain immune to these processes, and its anatomy and function are affected by hypertrophy, involution, or degeneration.

Malignant Disease in Old Age. F. McKeown. Brit. J. Cancer 10:251-256 (June) 1956 [London].

In autopsy studies on 1,300 patients dying over the age of 70 years, heart disease ranked first and cancer second as a cause of death. Twenty-five per cent of patients in the series had malignant disease, and this proved fatal in 20%. Males were affected more frequently than females, confirming the findings of other workers on the sex incidence of carcinoma in later life. The incidence of tumors rose slightly in the eighth decade as compared with the seventh, but this was partly accounted for by the increasing incidence of carcinoma of the prostate with age. The commonest site for a malignant tumor was the large intestine, 22% of all tumors occurring in this situation. The second most common tumor was carcinoma of the prostate, accounting for 14% of all malignancies. Tumors of the stomach, lungs, esophagus, bladder, kidney, and pancreas followed in that frequency, and rare tumors were those of cervix and ovary, thyroid, and melanoma. Nevertheless, most sites were represented. Of all the malignant tumors discovered, 20% were incidental in that they were unsuspected and did not contribute materially to the death of the patient. This emphasizes the importance of complete postmortem examination as the only means of determining the true incidence of any tumor.

RADIOLOGY

The Use of Tantalum 182 in the Treatment of Early Bladder Carcinoma. P. J. van Miert and J. F. Fowler. Brit. J. Radiol. 29:508-512 (Sept.) 1956 [London, England].

The authors review the methods available for dealing with early carcinoma of the bladder and suggest that more attention should be paid to the possibilities offered by interstitial irradiation, particularly in the matter of uniform and adequate dosage to the lesion-bearing area and the reduction of dosage to unaffected areas of bladder to a minimum. They describe new methods of using radioactive tantalum (Ta ^{182}) wire to achieve these ends. Ta ^{182} wire is used in straight lengths with the terminal centimeter twisted on itself to form a loop for attachment of the withdrawal thread. Introducing needles are modified from serum needles by first removing the syringe fitting and then machining a longitudinal slot in the whole length of the needle. A small circular tab is fitted to the proximal end for handling purposes and to act as a guard against complete insertion into the tissues. The needles have a uniform slight curvature concave towards the longitudinal slot. Special holding forceps are used in order to avoid crushing the introducing needles. Balloon catheters are used.

Of the two methods described, one is used for interstitial implantation from within the bladder lumen and the other for interstitial implantation of the bladder from its exterior aspect in association with partial cystectomy. The use of each method is illustrated by a case history. The second method of performing a tantalum wire implant could well be used for fundal lesions without doing partial cystectomy. A small incision could be made in the bladder to allow one finger to be introduced into the lumen to palpate the lesion and act as a guide while implanting the affected area, the needles then being inserted in the bladder wall from its exterior aspect. Suprapubic drainage could be dispensed with and a balloon catheter of the Foley type left in the urethra. Special attention was given to the problem of uniformity of dosage, and observations made on dosage control are described.

Angiocardiographic Demonstration of Inoperability in Some Cases of Pulmonary Neoplasia. F. Soave and B. Possenti. Minerva chir. 11:793-798 (Sept. 15) 1956 (In Italian) [Turin, Italy].

The authors made a study of the value of angiocardiography as a means of establishing the operability of pulmonary neoplasms. Observations on 27 patients with pulmonary tumor from the periphery to the hilum are reported. A tumor in the hilar and parahilar regions can affect the vessels either by compression or by invasion. In case of compression the vessels show changes in the pattern, and in cases of invasion the morphology and the course of the affected vessel are markedly affected. Compression was found in 20 patients who were operated on on the basis of radiographic findings. The contrast medium showed invasion in the remaining seven patients. Thoracotomy confirmed the inoperability of the lesion.

BOOK REVIEWS

Atlas cerebri humani: The Inner Structure of the Brain Demonstrated on the Basis of Macroscopical Preparations. By E. Ludwig and J. Klingler. [In English, French, German and Italian.] Cloth. $18.50. Pp. 36, with 100 plates. Little, Brown & Company, 34 Beacon St., Boston 6; S. Karger AG., Arnold Böcklinstrasse 25, Basel, Switzerland, 1956.

The atlas contains a series of photographs of macroscopic specimens of the brain, prepared by the Klinger method of fixing in a formaldehyde solution, freezing, and dissecting while moist with special instruments. The freezing tends to spread the nerve fibers and, thus, makes them easier to handle. The photographs were taken with a Leica camera and enlarged to about 10 by 18 cm. Tracings, with the legend, mostly from Parisiensia Nomina Anatomica, adopted by the International Congress of Anatomy in Paris on July 30, 1955, accompany each plate. The text, which precedes the plates, gives details of the Klinger technique and the nomenclature used and is in German, French, English, and Italian. These excellently prepared specimens, known to anatomists for over 20 years, are reproduced so satisfactorily that the atlas will be indispensable for demonstrating the gross tracts of the brain in classes in anatomy. There is a good index and an up-to-date bibliography. The previous atlas (1938) by the same authors has long been out of print.

United States Army in World War II: The Technical Services. The Medical Department: Hospitalization and Evacuation, Zone of Interior. By Clarence McKittrick Smith. Cloth. $4. Pp. 503, with illustrations. Office of Chief of Military History, Department of the Army; Superintendent of Documents, Govern. Print. Off., Washington 25, D. C., 1956.

This is one of a series of volumes on the history of the medical department of the U. S. Army during World War II. It deals primarily with the logistics of hospitalization and evacuation in the zone of the interior. The professional care of patients is not discussed here but will be discussed by specialists in future volumes of this series. When the President proclaimed a limited national emergency Sept. 8, 1939, the Army medical department was operating only 7 general hospitals and 119 smaller station hospitals. The gigantic task before the medical department to meet the requirements of World War II is revealed in the fact that between January, 1942, and August, 1945, there were 8,900,000 admissions to Army hospitals in the zone of the interior. In the same period, more than 518,500 patients were debarked at seaports and 121,400 at airfields in the United States for transportation to hospitals. By the end of June, 1945, the number of patients on the rolls of Army hospitals in the United States rose to more than 318,000. How the medical department met this unprecedented task of hospitalization and evacuation is the subject of this volume.

Pharmacognosy: The Study of Natural Drug Substances and Certain Allied Products. By Robertson Pratt, Ph.D., Professor of Pharmacognosy and Antibiotics, University of California School of Pharmacy, San Francisco, and Heber W. Youngken Jr., Ph.D., Professor and Chairman for Pharmacognosy, University of Washington College of Pharmacy, Seattle. Second edition. Cloth. $10. Pp. 694, with 70 illustrations. J. B. Lippincott Company, 227-231 S. Sixth St., Philadelphia 5; 2083 Guy St., Montreal, Canada; Pitman Medical Publishing Co., Ltd., 39 Parker St., Kingsway, London, W.C.2, England, 1956.

This edition, as was the previous one published in 1951, is intended primarily for students of pharmacognosy and for practicing pharmacists. Various sections have been expanded due to the developments in such fields as the antibiotics and the tranquilizing drugs. The section on agents used for the control of insects has been enlarged to include toxicity and emergency treatment of poisoning caused by some of the newer insecticides of the organic phosphate group. An appendix, listing some of the common plants that exist in the United States, has been added to this edition, and it provides information on the treatment of accidental poisoning caused by them. In addition to providing a useful text for students of the pharmaceutical sciences, the book should be of value to physicians and to others interested in the study of natural drugs and allied materials.

Jews in the World of Science: A Biographical Dictionary of Jews Eminent in the Natural and Social Sciences. Edited by Harry Cohen and Itzhak J. Carmin. Contributing editors: J. Robert Oppenheimer, Meyer W. Weisgal, and Louis Gershenfeld. Cloth. $18. Pp. 263. Monde Publishers, Inc., P. O. Box 209, White Plains, New York, 1956.

In his preface Dr. Cohen quotes the famous statement of Pasteur to the effect that "la science n'a pas de patrie." He then proceeds to argue not only that science can have a fatherland but also that it can belong to a definite group—in this instance the Jews. There are tributes to Albert Einstein, Chaim Weizmann, Jonas E. Salk, and others. It apparently did not occur to the writer that, were it not for the great Ehrlich, also a Jew, there would be no Salk. The founder of the science of immunity, Ehrlich, is not mentioned anywhere in the volume and neither is Metchnikoff, who first described phagocytosis. On the other hand the names of physicians, whose only contribution to science was that they were born Jews, are included. The value of this opus to science, and for that matter to the Jews as a group, may be questioned in view of such limitations.

Pelvimetry. By Herbert Thoms, M.D. Cloth. $5. Pp. 120, with 45 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1956.

This small book presents a practical description of the variations and abnormalities of the bony pelvis in relation to labor and describes certain diagnostic procedures by which pelvic morphology and pelvic capacity can be ascertained. Thoms' has devoted a large part of his career to this subject. He was a pioneer in urging that all primigravidas have a combined clinical and roentgenologic survey of the bony pelvis. The book is the culmination of the author's numerous contributions to the literature in the past 25 years. It is well printed in clear type, and most of the illustrations have been clearly reproduced. A few of the line drawings lack the professional touch. Nevertheless, the book is a classic and should be diligently studied by all obstetricians and roentgenologists.

Thiopentone and Other Thiobarbiturates. By John W. Dundee, M.D., F.F.A.R.C.S., D.A. Cloth. $5. Pp. 312, with 59 illustrations. E. & S. Livingstone, Ltd., 16 and 17 Teviot Pl., Edinburgh 1, Scotland; Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1956.

This book should rapidly come to be considered one of the classics in the literature of anesthesia. The author has condensed into a relatively few pages the pertinent mass of literature that has accumulated on this vital subject. This book is logically and clearly prepared in a fashion that makes it easy and pleasant to read, yet it is definitely informative. Although the author does not hesitate to express his opinion, he gives due consideration to the controversial aspects of the subject and, in the final analysis, presents the reader with the known as well as the unknown of the subject of anesthesia. This book is organized into 12 chapters dealing with history; physical properties and chemistry; distribution and fate in the body; the effects of thiobarbiturates on the body; variations in response to thiobarbiturates; the use of thiopental sodium in certain pathological conditions; hazards, therapeutic uses, and administration of thiopental; some newer thiobarbiturates; and analeptics and other stimulants. There are excellent references given on each aspect of the subject. The conciseness and neatness of this book's organization should make it valuable as a reference book for all who are interested. It can, therefore, be recommended to libraries, anesthesiologists, surgeons, pharmacologists, and physiologists.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

QUERIES AND MINOR NOTES

STRENUOUS EXERCISE IN OLDER PERSONS

To the Editor:—*Please give the consensus among physicians of the advisability of strenuous exercises (such as weight lifting, running, or dancing—all of them up to a point short of exhaustion or even fatigue) in a healthy man in his early fifties.* *M.D., New York.*

This inquiry was referred to two consultants, whose respective replies follow.—Ed.

Answer.—If the man in his early fifties is healthy, strenuous exercise such as weight lifting, running, and dancing is not harmful. An individual's general health has great influence on his tolerance for such exercise. If he can tolerate it well, it is not believed there is any harm in following a program of activities of this kind. Care should be taken with regard to exercise for an individual whose health shows some defect.

Answer.—There is no known study providing evidence as to a consensus on the question. The following excerpts from a from a committee report in *Hygeia*, August, 1943, are pertinent.

> Among older persons (over 40) physical examinations and observation of the individual's reaction to exercise will disclose large numbers who need to restrict exercise.
>
> Individual variations in capacity for exercise are important. Some persons, even at early ages, react unfavorably to exercise through extreme exhaustion, breathlessness and emotional depression. It is not wise to expect these persons to reach the same level of physical achievement as do those to whom exercise is an exhilarant and a stimulant.
>
> Hard, fast, sustained or highly competitive games and sports should not be played by persons beyond the age of 35, unless they have been playing them continuously and have kept themselves fit and accustomed to these sports.
>
> The ability to recuperate after exercise is a good guide at any age. Recuperation should be reasonably prompt. If breathing and heart rate are still greatly accelerated at the end of ten minutes after exercise, and if there is marked weakness or fatigue persisting after a two hour rest period, restlessness after retiring for the night with broken sleep, or a sense of definite fatigue the day following, the exercise has been too severe or too prolonged for that person in his present stage of training and physical strength.
>
> Exercise should be graded according to age, capacity of the individual, and the state of his training and fitness. In general, exercise should be modified in the direction of less strenuous activities after the age of 40.
>
> Since performance in any activity is fundamentally conditioned by the age, sex, and physical capacity of the participants, it follows that the amount of effort actually exerted by each individual will more significantly determine the contribution of the activity to his physical fitness than will the rules or other specifications that give form to the activity.

TRICHOMONAS INFECTION

To the Editor:—*Please suggest treatment of chronic urinary infection with trichomonads as the chief offending organisms. I have tried all the available antibiotic agents. Tritheon was also used.* *M.D., Florida.*

Answer.—It is taken for granted that the patient in question is a female. Infection in the urinary tract with trichomonads is usually of vaginal origin, and an attempt should first be made to eliminate vaginal infection. As is well known, this may be difficult to accomplish. Numerous trichomonacidal agents are available, but few, if any, seem to eliminate this organism permanently. The patient may have symptomatic relief and the trichomonads may disappear temporarily, but if subsequent vaginal cultures are made they are usually found to be present. It is particularly difficult to eliminate them, when present in the Skene's or Bartholin's glands. In the treatment of trichomonas infection, attention must be given to the male partner, and on examination of the semen in such cases trichomonads will be found in a high percentage of cases. Simultaneous treatment of both wife and husband should be given if the latter is found to be the carrier. Although Tritheon (2-acetylamino-5-nitrothiazole) has not been of value in this case, many observers have found it to be quite efficacious when administered to both the male and the female involved.

In this case, the chief problem seems to be a chronic urinary infection. While trichomonads often are found in the urine of patients suffering with vaginal trichomonas infections, they may be incidental invaders and cause little or no urinary symptoms. If there is definite evidence of chronic urinary infection present, the etiological organism is probably other than trichomonal. It would be necessary to have cultures made of the urine to determine the types of bacterial infection present. Such infection may be caused by a variety of lesions involving the urinary tract, which will have to be identified. As with every chronic urinary infection, a thorough and careful examination of the urinary tract, including cystoscopic examination with catheterization of the ureters and urographic examinations, is indicated.

CAUDAL ANESTHESIA IN OBSTETRICS

To the Editor:—*Does Hingson still use caudal anesthesia in obstetrics, or does he now prefer the saddle block method? Is there any center in the eastern United States where the Hingson caudal method is taught? At a local hospital the trocar and catheter method is used with a high percentage of failures. Is this method recommended in preference to methods with flexible needle?* *M.D., Massachusetts.*

Answer.—During 1955, continuous caudal analgesia was administered in the department of anesthesia at the University Hospitals of Cleveland 625 times, of which 595 uses were for obstetric labor and delivery. Saddle block spinal anesthesia was administered 2,558 times in obstetrics on the same service. "Anesthesia for Obstetrics," by Hingson and Hellman (Philadelphia, J. B. Lippincott Company, 1956, p. 182) contains statistical data from 8,000 consecutive labors and deliveries supervised by Hingson and his staff, in which 28% of the private patients and 16% of staff patients in Johns Hopkins Hospital had caudal analgesia, with spinal being used in 13%; whereas the adjoining Sinai Hospital utilized caudal analgesia in 18% and spinal in 60%. Caudal analgesia is to be preferred for patients with systemic diseases and for primiparas undergoing long hours of labor, provided that the caudal is instituted after 5 cm. of cervical dilatation for precipitous or rapid labors, with systemic sedation preliminary to a low-dose spinal anesthesia for delivery. Continuous caudal analgesia is being used for the majority of cases in the Beth El Hospital in Brooklyn, N. Y., and for a large percentage in the Mount Sinai Hospital in Manhattan. More than 60 centers in the United States use this method regularly; for example, the maternity service at Fort Sam Houston, Texas, has conducted more than 16,000 deliveries with this technique. Many anesthesia residencies are teaching this method, for example, Columbia University Hospitals, Manhattan; Western Reserve University, Cleveland; Mason Clinic, Seattle; and Stanford University, San Francisco. At the present time, there are no intensive courses on this subject being given for short periods.

CHLORINATION OF WATER

To the Editor:—*What measures should be taken in a small community in which the municipal water samples are returned from the state laboratory frequently as being unsafe "due to high coliform count"? These samples are unsafe in spite of apparently adequate chlorination. There have been sporadic cases of typhoid in this area.* *M.D., Colorado.*

Answer:—A chlorinated municipal water supply that continually has specimens showing high coliform indexes is either one using water of a quality for which simple chlorination is not a satisfactory method of treatment or one for which the methods of application and control used are inadequate. On the

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

basis of the limited information given, these two points are to be considered: 1. Certain sources of water have a high color and turbidity and contain a large amount of organic and inorganic matter and a high bacteria content. Simple chlorination cannot be successfully used in such cases. Here other types of treatment are indicated, such as coagulation and filtration, supplemented with chlorination. 2. If the source water is of satisfactory quality for simple chlorination, then, to be effective, chlorine must be added under controlled conditions, that is, by trained personnel, with adequate equipment and properly selected points of application. A knowledge of the chlorine demand of the water is necessary so that, when chlorine is added, the proper amount is used to satisfy this demand and still to leave a residual of approximately 0.5 ppm in the most remote part of the distribution system.

The above conditions may change periodically, hence, it is imperative to control the addition of chlorine and make regular residual chlorine tests, at least daily. It is suggested that, in organizing the control methods, the assistance of a qualified sanitary engineer be obtained. Regarding the advisability of mass typhoid inoculations, the local and state health authorities should be consulted.

EXPOSURE TO TRICHLOROETHYLENE

To the Editor:—*Is prolonged exposure to trichloroethylene vapor likely to cause renal damage?*

M.D., South Carolina.

Answer.—The current belief is that trichloroethylene seldom leads to renal involvement. This statement applies alike to acute and chronic poisoning. In fact, there is wide denial that a chronic state arises and affirmation that trichloroethylene does not lend itself to cumulative effects. Johnstone categorically states: "The kidneys or liver are not commonly injured by trichloroethylene." The following statement is taken from Browning: "Most authorities appear to consider that nephritis as a sequel is unknown. Stüber (1931) states that the kidneys are never affected. Roholm (1933), however, mentions acute nephritis as a manifestation of severe poisoning." Von Oettingen makes these observations in connection with animal experiments: "With regard to pathological changes in the kidneys, Wright and Schaffer (1932) noted in dogs after oral doses of 5 cc. per kg. cloudy swelling and congestion of these organs. Bose and Mukerji (1944) reported no liver injury but signs of acute toxic nephritis. Lehmann and Schmidt-Kehl (1936) saw, after repeated exposure of rabbits, cloudy swelling and hyperemia with fatty infiltration. Similar findings were reported by Herzberg (1934), and Dervillée, Nun, and Casts (1939) saw regularly, lesions in the convoluted tubules of rabbits after oral doses, whereas the glomerular apparatus was not affected." From industrial exposure renal damage is practically unknown, and the same statement applies to the use of trichloroethylene for anesthetic purposes. The foremost locus of action of trichloroethylene is the central nervous system.

STINGING TENTACLES OF JELLYFISH

To the Editor:—*What is the "stinging" chemical that one contacts with the tentacles of the "sting nettle" of the Chesapeake Bay? This marine animal is of the jellyfish family and abounds in the water near the rivers of the tidewater region. What is the best medicament to apply to the skin after contact, to relieve the stinging pain? What precautions and what medicament should be used when a swimmer's eyes have been "stung"? Is there any method for ridding the water of these creatures?*

Harold W. Felton, M.D., Deltaville, Va.

Answer.—Studies on extracts of coelenterate tentacles indicate that the pain-producing factor is probably 5-hydroxytryptamine. The concomitant paralysis may be due to two or more related quaternary ammonium bases such as tetramethylammonium and urocanylcholine. Treatment of coelenterate stings should be directed toward accomplishing their primary objectives: relieving pain, alleviating neurotoxic effects, and controlling primary shock. Morphine sulfate is effective in relieving pain. Calcium gluconate 4 gives prompt relief of muscular spasms; oral antihistaminics and topical creams afford alleviation of urticarial lesions and symptoms as do ammonium hydroxide, sodium bicarbonate, olive oil, and ethyl alcohol. Artificial respiration, cardiac and respiratory stimulants, and other supportive measures may be required. If a swimmer's eyes should be stung, any one of the remedies mentioned above that would not be harmful by itself may be used. There is no practical method of ridding the water of noxious coelenterates. Avoidance of the animals, whether in the water or on the beach, is the best prophylaxis.

SURGERY OF FALLOPIAN TUBES

To the Editor:—*What is the approximate percentage of pregnancies obtained after surgery on fallopian tubes? Does the procedure for repair of a tubal closure depend to a certain extent on where the tubes are closed? What procedure can be considered favorably? What is the percentage of ruptured fallopian tubes and the percentage of serious hemorrhages?*

Howard Starret, M.D., Cuernavaca, Morelos, Mexico.

Answer.—A year ago Siegler and Hellman summarized the results of salpingoplastic operations in the practices of 734 qualified specialists. Pregnancy occurred in 22.6% of the cases reported. Of the pregnancies obtained, about 15% terminated in abortion, 9% in ectopic gestation, and 74% in live births. The high incidence of extrauterine pregnancy, is, unfortunately, a feature to be expected in a group of cases in which the tubes are more or less damaged. Rupture and serious hemorrhage should rarely happen in women who are under the close observation of competent gynecologists. The chances of success are greatest when the obstruction is located at the fimbriated ends of tubes not otherwise notably affected by inflammatory disease. Of 77 operations performed by this consultant in similar cases, 28 resulted in the birth of living children. Each of the newer techniques for maintaining patency postoperatively has at least theoretical advantages, together with some disadvantages. After salpingostomy for fimbriated-end occlusion, this consultant relies mainly on early and repeated injection of iodized oil and insufflation of gas.

PERFORATION OF CORNEA

To the Editor:—*Occasionally, I have had to remove deeply embedded foreign bodies from the cornea under local anesthesia produced with Dorsacaine. At times, I have had to scrape gently but deeply with an eye spud to get all the particles out. Suppose I perforated the cornea on one of these attempts. How should I treat such an injury if it did occur? I am not an eye specialist, and I am 40 miles from the nearest medical center.*

M.D., Oregon.

Answer.—The cornea is surprisingly resistant to perforation with an eye spud. A more common complication than perforation is pushing the foreign body through the cornea into the anterior chamber. If this occurs the pupil should be constricted, provided the foreign body is anterior to the iris. Then the patient should be transported to special care, with the head in such a position that the foreign body cannot go through the pupil into the interior of the eye. If the anterior chamber is entered with an eye spud, there is a sudden loss of aqueous, which causes the iris to touch the cornea. Usually the opening is so minute that it is closed by fibrin in the reformed aqueous and the eye quickly heals. Immediately following such a perforation, it is advisable that both eyes be patched and that the patient be placed supine on a litter and transported by ambulance to the closest eye specialist.

DRUGS INTERFERING WITH PROTEIN-BOUND IODINE DETERMINATION

To the Editor:—*I would like a list of drugs that contain the iodide radical capable of giving a disturbed protein-bound iodine level.*

John D. Lynch, M.D., Manitowoc, Wis.

Answer.—Organic iodine-containing compounds known to effect protein-bound iodine determinations include iodine-containing radiopaque dyes used in angiocardiography, cholecystography, urography, bronchography, or myelography; iodinated amebicides (chiniofon, iodochlorhydroxyquin, and diiodohydroxyquin); vaginal suppositories such as Floraquin, which contains diiodohydroxyquin; penicillin G diethylaminoethyl ester hydriodide (Neo-Penil); and iothiouracil. Preparations containing inorganic iodine include Lugol's solution, tincture of iodine, and syrup of hydriodic acid. Certain vitamin and cod liver oil preparations may also be rich in iodine, while barium sulfate is said to give rise to elevated protein-bound iodine due to contaminating iodine. Sulfobromophthalein (Bromsulphalein) dye, though not containing iodine, also causes elevation of plasma protein-bound iodine. Due to the widespread use of iodide-containing compounds and the frequent difficulty of obtaining a history of exposure to such drugs, some laboratories now determine inorganic iodine in addition to protein-bound iodine, as an aid to the detection of spuriously high values.

PREDNISONE FOR ASTHMA

To the Editor:—*A 10-year-old boy has had bronchial asthma every fall since he was one year of age. The usual drugs for wheezing—ephedrine, aminophylline, adrenalin, and sedatives—have little effect in terminating his attacks, but doses of 2.5 mg. of prednisone given eight hours apart for nine doses clear up the attacks. He is being desensitized against inhalants and foods. Is it better to use prednisone each time an attack occurs or to treat with the usual bronchodilators? Would it be of any advantage to keep him on therapy with 5 mg. of prednisone daily during the fall season?*

A. McCray Jones, M.D., Whaleyville, Va.

Answer.—Considering the ineffectiveness of the usual medication and the response to small doses of prednisone in this case, it would certainly be better to use the latter when an asthma attack occurs. Whether one should give the prednisone during the entire fall season would depend somewhat on the history of the boy's reaction to the drug. If he is symptom-free for some time after the hormone is used, it would be preferable to use it only when a new attack occurs. If, however, symptoms tend to persist and moderate doses keep the boy well, it is perfectly proper to use it during the entire season.

ABSENCE OF THE APPENDIX

To the Editor:—*An 8-year-old boy with a diagnosis of chronic appendicitis was operated on. A McBurney incision was made and no appendix appeared, though the incision was enlarged twice. The cecum was normally placed, and at the junction of the ilium and the cecum there was only a rich vascularization without any trace of appendix. The chief surgeon's help was immediately requested and after a half-hour's search, following my own search for an hour, the abdomen was closed with no appendix having been found. How can this be explained?*

Juan Rodriguez, M.D., Matanzas, Cuba.

Answer.—Granting that the retrocecally placed appendix can lie subserosally along the cecum and can be difficult to find, it seems doubtful from the description given that such was the case. Congenital absence of the appendix is apparently quite rare, but occasional cases have been reported. Spivack (Am. J. Surg. 13:297, 1931) has felt that some cases of this type represent hypoplasia rather than actual agenesis of the appendix. Perhaps this patient presented the very rare instance of congenital absence of the appendix.

ZINC DEFICIENCY AND LEUKEMIA

To the Editor:—*Is there any scientific evidence to support a statement in the lay press that there appears to be a definite relation between leukemia and a deficiency, probably dietary, in the so-called trace elements, especially zinc?*

W. B. Cox, M.D., Missoula, Mont.

Answer.—There is no evidence that a deficiency of a trace element such as zinc causes leukemia. The statements in the lay press referred to in the query may have been derived from findings that some leukemic cells contain less zinc than normal leukocytes. Leukemic cells (as neoplastic cells in general) are poor in some normal components; e. g., myeloid leukemic cells contain less alkaline phosphatases than normal cells but this is no proof of causal relationships. Concerning zinc in leukocytes, see Bert L. Vallee, Trace Elements and Pathologic States, in "Principles of Internal Medicine" (Harrison, T. R., and others, editors, New York, Blakiston Company, 1954).

RESEARCH REVIEWS

From time to time there will be published in this section of The Journal *brief but not necessarily complete reviews of some of the newer clinical aspects of medical research and practice. This material is gathered specifically for* The Journal.—Ed.

VIRUSES

New laboratory techniques have led to the identification of many previously unrecognized viruses. In fact, the problem today is no longer isolation and recognition of new viruses but to know whether they cause disease.

A meeting that was held recently is characteristic of the present situation. Its title was "Conference on Viruses in Seach of Disease."[1] Among the viruses recently discovered are a group found in the respiratory tract and conjunctivas of man, which has been referred to by various names: adenoid degenerative (AD), later called adenoidal-pharyngeal-conjunctival (APC) viruses; respiratory illness (RI) agents; acute respiratory disease (ARD) group. To avoid confusion, some of the investigators active in this field met in New York in May and decided to replace all these names by the term adenovirus.

So far, more than 500 strains of adenoviruses have been isolated. They have been grouped together into serologic types; 13 of these types have been identified in material from human sources.[2]

The question whether they cause clinically manifest disease has been answered for some of these serotypes: Hilleman[3] pointed to the etiological relation between RI-67 and respiratory disease in 1954. He showed that RI-67 (now known as adenovirus type 4) was associated with acute respiratory disease (ARD) and primary atypical pneumonia (PAP) among soldiers. It is now known that types 3, 4, and 7 cause acute febrile respiratory illnesses in young adults.[4]

At the National Institutes of Health in Bethesda, Md., adenovirus type 3 was recognized as the cause of pharyngoconjunctival fever,[5] a syndrome characterized by pharyngitis, conjunctivitis, fever, malaise, and cervical adenopathy. Type 3 has been found in persons of all age groups.

Less certain is the causal relation between acute febrile upper respiratory tract illness and adenovirus types 1, 2, and 5. These serotypes occur mostly in infants and young children. The multiplicity of infecting agents and the frequency of febrile illnesses in this age group complicate the problem.[2]

It is thought that the conjunctivas may be the portal of entry in some cases. Adenovirus types 6 and 8 appear to be specifically related to ocular disease, type 6 to follicular conjunctivitis and type 8 to keratoconjunctivitis.

Recognition of an etiological relation between adenoviruses and clinical disease has led to attempts at protecting those most exposed to these infections by vaccination. A type 3 vaccine prepared in the laboratory was tested in young adult volunteers.[6] It gave satisfactory protection.

At the Walter Reed Army Institute of Research, Washington, D. C., a bivalent (types 4 and 7) vaccine was prepared and found to be highly effective in reducing the incidence of acute respiratory illness of adenovirus etiology in recruits.[7]

A joint study with use of a commercially prepared trivalent (types 3, 4, and 7) vaccine has been in progress since December, 1955. The Naval Medical Research Unit Nr.4, the National Institutes of Health, and the University of Chicago have been cooperating. The vaccine has been given by a single intramuscular injection to about 4,000 naval recruits; another 12,000 recruits served as controls. Of these, about one-third have completed their training. Analysis of the results obtained in this group shows that the vaccine gave protection in a significantly high proportion. There were no local or general reactions following inoculation.[8]

There has been progress also *in elucidating the etiological role of other viruses.* At the meeting mentioned above, A. J. Rhodes,[9] the Hospital for Sick Children, Toronto, reported that Coxsackie viruses of Dalldorf's group B have been found to be a cause of aseptic meningitis in children. It has been known for some time now that these viruses are also associated with pleurodynia. H. M. Meyer Jr. and his co-workers,[10] the Central Virus Diagnostic Laboratory for the Armed Services, Walter Reed Army Institute of Research, Washington, D. C., recovered Coxsackie viruses group B and orphan viruses from specimens from the alimentary tract of patients with clinical cases of aseptic meningitis. Three of the four Coxsackie viruses found belonged to serotype B-3 and the other to serotype B-2. The 13 orphan viruses recovered fell into three serologic groups: Walter Reed 1, 2, and 3. Eleven of the orphan viruses found were in the WR-1 group, the rest in groups WR-2 and WR-3. *A comparison* between WR orphan strains and ECHO viruses was made: It was found that WR-1 was related to ECHO-6, and WR-3 to ECHO-2. After having carefully excluded other agents known to cause aseptic meningitis, these workers believe that these viruses are etiologically related to the disease. They were recovered during the acute phase of the illness and there was a significant increase in specific antibody during convalescence. Specimens in this investigation came from widely separated areas: Massachusetts, the area around Washington, D. C., Florida, and California. It is of importance that these viruses may be definitely considered to be a cause of aseptic meningitis clinically indistinguishable from nonparalytic poliomyelitis

R. H. Parrott,[11] National Institutes of Health, Bethesda, Md., recovered Coxsackie virus group A from 84% of cases of herpangina (vesicular pharyngitis). In his opinion these viruses are associated with the disease. The serotypes isolated have been consistently the same six: A-2, A-4, A-5, A-6, A-8, and A-10. Most cases of herpangina can be distinguished clinically from gingivostomatitis.[12]

In the field of *chemotherapy* of virus diseases one of the difficulties has been that selective poisoning of the parasite without harming the host presents problems different from those encountered in some bacterial diseases. This was pointed out by F. M. Schabel Jr.,[13] Southern Research Institute, Birmingham, Ala., who recently reviewed the subject. He thought that exploitable biochemical differences between host cells and viruses may lie in protein and nucleic acid metabolism. While viruses reproduce at the expense of the host cells, using their energy sources and building blocks, they put the building blocks together in a different way, forming different proteins and nucleic acids. Experimental work with compounds derived from antibiotics promises to lead to a better understanding of these mechanisms. Noformicin (Mk-61) obtained from Nocardia is active in mice and eggs against human influenza virus (types A, A′, B) and against swine influenza; in eggs it is active against mumps and Newcastle disease virus. Ehrlichin and Netropsin derived from Streptomyces are active against influenza (type B) and vaccinia (WR strain). The toxicity of some of these compounds in man is an obstacle to their therapeutic use.

At another meeting, P. K. Smith and his associates,[14] the George Washington University, Washington, D. C., presented papers on the action of canavanine flavianate, which inhibits the growth of influenza A virus (WS strain) in tissue cultures of dispersed chick embryo lungs, and on compounds in the thiosemicarbazone and diphenyl group. Ten of these and related substances showed significant action against influenza virus, strain A, PR8. Seven drugs were tested by oral feeding to mice, beginning one day prior to infection; some of these gave appreciable protection. All control animals in this experiment died within eight days.

Strenuous efforts are being made at present in a rational approach to virus chemotherapy. Thousands of compounds have already been tested in many research centers. So far, none are known to hold definite promise of clinical success.

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« Washington News »

Health Legislation High on Congressional Agenda • •
24 Million to Help Build Research Plants • •
VA Reports Better Use of Mental Hospital Space • •
Library of Medicine Reports on Year's Activity • •

HEALTH LEGISLATION

As newly elected members of the 85th Congress and holdover members from the 84th assemble in January for another two years, health legislation will be high on the domestic agenda. On the health list, in turn, three proposals now stand out above all others. They are federal grants for medical school construction, federal employees health insurance, and pooling arrangements to stimulate insurance companies to broaden voluntary health plans.

Whether these and other health proposals are enacted this session will depend in some degree on the administration's desire to push them in the face of new demands on the federal treasury. The world situation has placed emphasis on dollars for defense.

Cognizant of this, Secretary Folsom says that, while "we must maintain this defense posture, we want to be very careful that we don't let down on expenditures in the field of health, education, and welfare." The Secretary of the Department of Health, Education, and Welfare adds: "We have also to look out for our human resources: To see that the people are well educated, that we cut down illness as much as we can, and that we also provide a sense of economic security for the older people."

Groundwork already has been laid for consideration of medical school aid. The staff of the House Interstate and Foreign Commerce Committee has prepared a report on background information relating to schools of medicine, dentistry, osteopathy, and public health. The report is an outgrowth of a questionnaire sent to more than 50 organizations and groups, in which they were asked to supply information on a wide range of subjects within the framework of medical education and physician supply.

The administration sought last session to get medical school construction aid made a part of the laboratory research facilities bill, but Congress decided to defer action. Now the way appears clear for a full-dress study of the question in the coming session.

Another proposal in which a vast amount of time and staff work has been expended is federal workers' health insurance. The Civil Service Commission is seeking a new approach that would combine earlier plans for both basic coverage and major medical expenses. The commission hopes to reconcile the conflicting views of nonprofit plans (Blue Cross and Blue Shield), of commercial carriers, and of federal employees unions.

The last effort, a proposal for major medical coverage with the government paying the premiums, failed to get through the 84th Congress after objections by nonprofit and union spokesmen. An even earlier plan for basic coverage with a sharing of premiums between government and worker foundered over the issues of administrative costs and the extent of government payment of premiums.

The third health item certain to be pursued, with strong administration backing, is Secretary Folsom's plan for allowing the pooling facilities of smaller insurance companies, which would be facilitated through the waiving of antitrust laws. The theory is that this would encourage companies to experiment in new fields, such as catastrophic insurance and plans for the aged.

This proposal is a substitute for the long-dormant reinsurance plan, under which the federal government would move into the health field through a federal reinsurance fund. In other words, it would guarantee losses up to a certain percentage for those companies that took out reinsurance and suffered losses because of experimentation. Mr. Folsom has indicated the administration still favors this in principle but admits chances of passage are slim. Congress rejected the idea two years ago.

There has been considerable activity already in the proposal for tax deferment of money paid by the self-employed into retirement plans—the Jenkins-Keogh type bills. The idea appears to have majority support among House members, but there could be one hitch: a reluctance of legislators in the final showdown to give preferred tax treatment when no general tax cut is in the offing.

Congress will have to take action in the military medical field before July 1, when the "doctor-draft" expires. In all likelihood the regular draft will be amended to provide the means for the orderly call-up of doctors and other scientific personnel under age 35 who have not served their time under the regular draft. The Armed Services are making efforts to encourage medical school graduates to take intern and residency training under a special deferment program in which doctors promise later active service.

Congress could enact no new legislation this session and it would still have to vote large sums of money for existing health programs. They include Hill-Burton hospital construction, laboratory facilities, public health and nurse training grants, water and air pollution control, and, looming larger than ever, money for more medical research. In the field of research, Congress has shown no inclination to slow down its giving.

RESEARCH FACILITIES GRANTS

Seventy-three grants totaling $24,460,467 have been awarded by the Public Health Service to help institutions build additional health research facilities under a program enacted at the last session of Congress. The law authorizes grants totaling 90 million dollars to be spent over three years at the rate of 30 million dollars annually. Money must be matched 50-50 by the recipient. Grants are approved by the surgeon general of

(Continued on page 22)

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Washington News—Continued

the Public Health Service, on recommendations of the National Advisory Council on Health Research Facilities.

In September, seven grants totaling $765,159 were approved. In approving the new group, the council deferred action on about 50 others. The next meeting of the council is scheduled for March. In announcing the awards, Surgeon General Burney explained that for the present the emphasis will be on construction grants, although the new law also authorizes grants to help in purchasing equipment. He said: "The approved grants were recommended by the council for the construction of research facilities and do not include funds for movable equipment. The council felt that, in order to get more facilities underway more rapidly with currently available funds, and in face of the large need as shown by the $66,888,239 in completed applications, and $49,160,774 in letters of intent from institutions desiring to apply for aid, it should provide awards this first year of the program for buildings. The council also felt that in the program's ensuing years assistance toward essential equipment for the research buildings can be provided."

The two largest of the new grants (each a million and a half dollars) went to Stanford University Medical School and the University of Utah College of Medicine for new research facilities buildings. Other large grants include: University of Alabama Medical Center, $1,033,500; California Institute of Technology, $477,000; University of Southern California, $854,000, Yale University, School of Medicine, $461,612; University of Miami, $941,720; University of Chicago, Division of Biological Sciences, $250,000; University of Kentucky, $1,208,992; Johns Hopkins University, $960,000; Retina Foundation, $300,000; New England Center Hospital, $400,000; Wayne State University, College of Medicine, $900,000; University of Michigan, School of Public Health, $605,000; University of Michigan, $600,000; Sloan-Kettering Institute for Cancer Research, $900,000; Roswell Park Memorial Institute, $646,000; Rockefeller Institute for Medical Research, $600,000; University of Buffalo, $463,020 (School of Medicine); University of Cincinnati College of Medicine, $865,688; Ohio State University College of Medicine, $900,000; University of Pittsburgh, $649,312, University of Pennsylvania, Medical Division, $400,000; Brown University, $411,002; and University of Wisconsin, Medical School, $975,000.

VETERANS HOSPITALS

The Veterans Administration reports that more efficient use of bed space has given it the equivalent of another 1,700-bed mental hospital in the past four years. In releasing the details, Dr. J. F. Casey, head of the VA's psychiatric and neurological service in Washington, D. C., said approximately that number of beds have been freed in mental hospitals since 1952 through transfer of elderly, chronic mental patients with physical illnesses to general and surgical hospitals that offer special care to aged patients.

All of the patients were moved to the hospitals nearest their homes staffed to give psychiatric as well as general medical treatment. The patient's consent was obtained in every case. Dr. Casey said the beds vacated in mental hospitals were filled immediately by veterans with acute mental illnesses who had been waiting admission. Patients transferred were described as "those whose mental illnesses had become stabilized and resistant to treatment for 10 to 20 years, so that their chronic physical illnesses were predominant."

NATIONAL LIBRARY OF MEDICINE

During the fiscal year that ended last June 30, the National Library of Medicine acquired 9,420 books, 69,367 serial pieces, and 1,130 new serial titles. The library was known as the Armed Forces Medical Library until this year, when Congress changed its name and placed it under the Department of Health, Education, and Welfare. In its annual report, the library cited these additional statistics: Spent $1,215,274 for all operations and employed a force of 209 persons, purchased 309 old and rare items for the history of medicine division, cataloged 19,841 titles; bound 12,824 volumes; added 2,417 pictures and portraits to its art collection, prepared 19,332 main entries for the 1955 volume of the library catalog; circulated 117,026 volumes, answered 6,722 reference questions; and filmed 1,499,075 pages in response to 83,972 photoduplication orders.

MISCELLANY

Brig. Gen. Harold Willard Glattly will retire early next year from the Army Medical Corps. He received the Legion of Merit for his "selfless performance to fellow prisoners" while in Japanese custody. . . . Salvatore G. DiMichael has been named New York City Regional Representative of the Office of Vocational Rehabilitation, Department of Health, Education, and Welfare . . . "New Perspectives for Research on Juvenile Delinquency," recently published by the Children's Bureau of HEW, is the report of a conference on the interrelation and relevance of sociological and psychiatric concepts to delinquency. It may be obtained from the Government Printing Office, Washington, D. C., for 30 cents a copy. . . . A federal court in Virginia has allowed an income tax deduction for the cost of installing a detachable invalid elevator, without medical advice, for a person suffering from osteoarthritis. The court stated that this was not an expenditure for capital improvement "but to lessen the aggravation of an existing condition." It did not discuss whether medical advice was a prerequisite for a medical expense deduction. . . . With President Eisenhower and Secretary Folsom urging the general public to have the three poliomyelitis shots, two large producers of Salk vaccine (Eli Lilly & Company and Pitman-Moore Company) announce substantial cutbacks in serum production. At present it is estimated 20 million poliomyelitis shots are in storage in the United States. . . . An employment profile of scientists in 1954 and 1955 has been released by the National Science Foundation. The report, based on data collected from 94,000 scientists, finds that 41% had Ph.D. degrees, 25% M.A. degrees, and 32% A.B. or first professional degrees. . . . The National Naval Medical Center at Bethesda, Md., received a plaque from the officers and men of the Pakistan Naval Hospital, Karachi, Pakistan, for assistance in providing training in various medical specialties for Pakistani officers. . . . The state of Texas and the United States Air Force recently held a joint conference on traffic safety to discuss ways of reducing traffic accidents among air force personnel on public highways.

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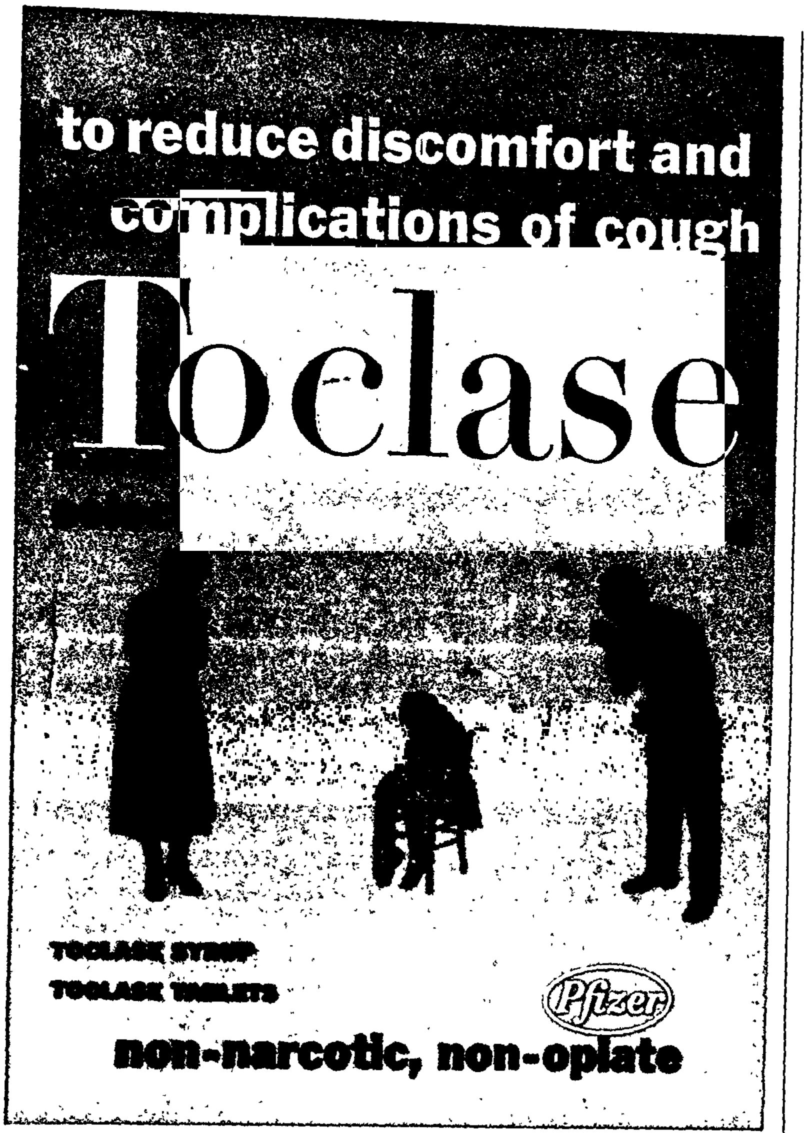

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THE JOURNAL

of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 162, NO. 18

CHICAGO, ILLINOIS

DECEMBER 29, 1956

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INDICATIONS FOR VACCINATION AGAINST POLIOMYELITIS

John R. Paul, M.D., New Haven, Conn.

• *Immunity to poliomyelitis comes about naturally and early in life in some unvaccinated populations. In others, high susceptibility prevails in all age groups so that severe epidemics involve children, parents, and grandparents. In the United States differences exist not only between states but even within cities, and in general the people in the poorest urban areas become immune early in life. It is a question whether vaccination with the killed antigen will prepare young people, for instance, to resist the risk young parents face when exposed to the infection by their own children. If it turns out that natural infection helps to keep up the individual's immunity, it may be necessary to have the feeding of live virus regularly follow the inoculation of killed vaccine. The invaluable start that has been made should not be regarded as the final technique of immunization against poliomyelitis.*

With the ever-increasing use in the United States of a formalinized (killed virus) antipoliomyelitis vaccine (the Salk vaccine), which now has been administered to many millions of children, one can entertain the reasonable hope that by the end of 1956 there will have been a substantial reduction in the annual quota of cases of paralytic poliomyelitis in this country. During the last 14 months, safety factors in the preparation of this vaccine seem to have been successfully controlled; it has been demonstrated that some degree of immunity to the most severe (paralytic) forms of this infection has been established in a large percentage of the vaccinees and this immunity may last at least one to two years. Among the important problems to be discussed are (1) how this vaccination will affect the rate at which and degree to which vaccinees acquire subsequent inapparent alimentary infections with polioviruses (the only evidences of these infections are the excretion of virus from the throat or intestinal tract and the coincidental development of antibodies) and (2) what the ultimate duration of immunity to paralytic poliomyelitis will be. Careful laboratory observations will soon answer the first question. Time will eventually answer the second.

Naturally Acquired Immunity

My approach to this problem will be to consider how immunity to poliomyelitis comes about naturally in populations unvaccinated against poliomyelitis and what leads can be obtained from such experience to indicate who should be vaccinated and how often. It is common knowledge that most of us have been infected subclinically, i. e., so-called alimentary infections with one or more types of poliovirus during childhood and thereby have gained our immunity. However, it is not common knowledge that reinfection of this kind, with the same type of poliovirus, can be readily induced artificially. Koprowski[1] and Sabin[2] have shown that individuals sometimes may be infected artificially more than once with the same type of attenuated poliovirus and, indeed, the same strain.

Practical questions about this are as follows: 1. How soon would one expect immunity to decline in persons vaccinated with the formalinized (Salk) vaccine according to the present schedules? Regardless of whether immunity declines rapidly or slowly, will a full course of revaccination, or a series of so-called booster inoculations be indicated in children, adolescents, and young adults every few years or so? 2. On the other hand, to what extent can one depend upon natural alimentary infections or reinfections in a vaccinated child to keep his or her immunity automatically in constant repair? By this I mean the maintenance of immunity against both severe and mild infections, not only for 5 or 10 years but for life. That paralytic infections may occur in a certain percentage of immunized vaccinees is recognized. Less is known about the prevalence of alimentary infections in vaccinees, but that such mild infections may occur (within 12 months of vaccination) is an established fact from field observations made by several groups in 1954 and 1955, although in 1955 the full course of vaccination was not given. That an alimentary infection may be experimentally induced in a vaccinee has been demonstrated at least once, when feeding

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From the Section of Preventive Medicine, Yale University School of Medicine.

Read before the General Scientific Meetings at the 105th Annual Meeting of the American Medical Association, Chicago, June 11, 1956.

of type 3 attenuated poliovirus was carried out in a child 9 years of age vaccinated one month previously with two doses of Salk vaccine. In this child, a postvaccinal alimentary infection was quickly established,[3] and virus was excreted for at least 39 days subsequently.

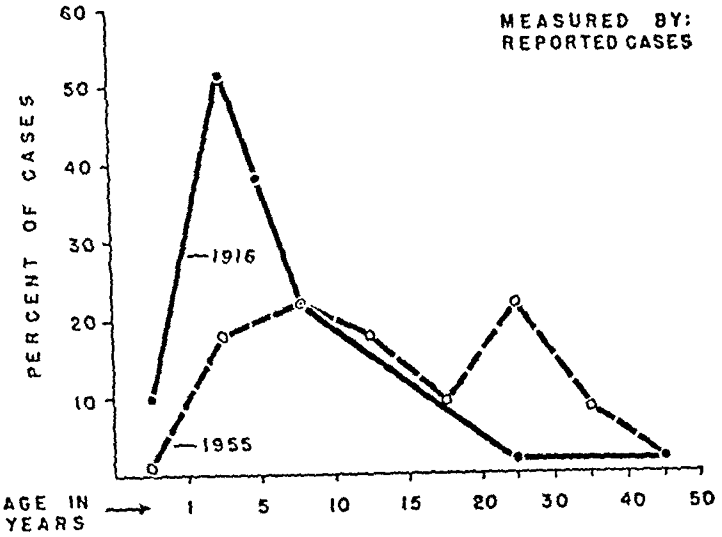

Fig. 1.—Comparison of age distribution of poliomyelitis cases in Connecticut in 1916 and 1955. (Data from Dr. James C. Hart and Dr. Mila E. Rindge, Bureau of Preventable Diseases, Connecticut State Department of Health, Hartford, Conn.)

Methods of Measuring Immunity

Before considering the role natural infections may play in the maintenance of the immunity of a vaccinated child, it seems worthwhile to review the status of immunity or susceptibility in various unvaccinated populations, both in this country and abroad. There are at present at least two ways of measuring immunity or susceptibility to this disease in a sample of a given population. One of these is by a serologic survey, the other by recording the ages at which clinical poliomyelitis infections occur. The former calls for testing of blood specimens for antibodies (against the three types of poliovirus). Such a sample should cover all age groups under 30 years and, I might add, may advantageously also cover groups representing different kinds of geographical or socioeconomic environments.

I do not have to emphasize here that presence of antibodies and immunity are not synonymous. Only indirectly does the presence of specific antibodies of a given titer in a previously infected or immunized individual suggest that the individual may resist subsequent poliomyelitis infection, provided he is not too heavily exposed to virus.

The second method of estimating immunity against poliomyelitis within a population is to record the ages at which clinical poliomyelitis is or has been actually acquired within a given period of time. If, for instance, all of the poliomyelitis cases recognized clinically within a given population are limited to children, this usually means that the local adult population is probably immune. An illustration of this approach can be found in figure 1, where the percentage of clinical cases of poliomyelitis in various age groups, as recorded in the state of Connecticut, in two different epidemic years (1916 and 1955) is charted. One can estimate how different the immune status was between these two populations, separated by a period of 40 years, by considering the differences in the age groups in these two series of patients. Correspondingly, the indications for vaccination might have differed in them. In one, that of 1916, the population was apparently solidly immune to paralytic poliomyelitis by the age of 20, while in the other, in 1955, immunity in the young adult population was far from solid, for there were many cases in the age period of 20 to 30.

One could go far afield here and point to geographical areas with inhabitants who have practically no immunity to poliomyelitis, such as those in arctic regions, where, so far, polioviruses have seldom penetrated; and others, in North Africa, where the local population is apparently exposed to an excess of virus throughout most of every year, and where immunity to both paralytic and alimentary infections is solid after the age of about 5 years. However, when poliovirus does penetrate into arctic areas and is given the opportunity to attack these highly susceptible "virgin" populations, we witness severe epidemics involving not only children but parents and grandparents as well. Indeed, it is the youngest group of children who apparently suffer the least under these circumstances. Such epidemics have been described on a few occasions in the Arctic, northern Canada,[4] and Alaska.[5]

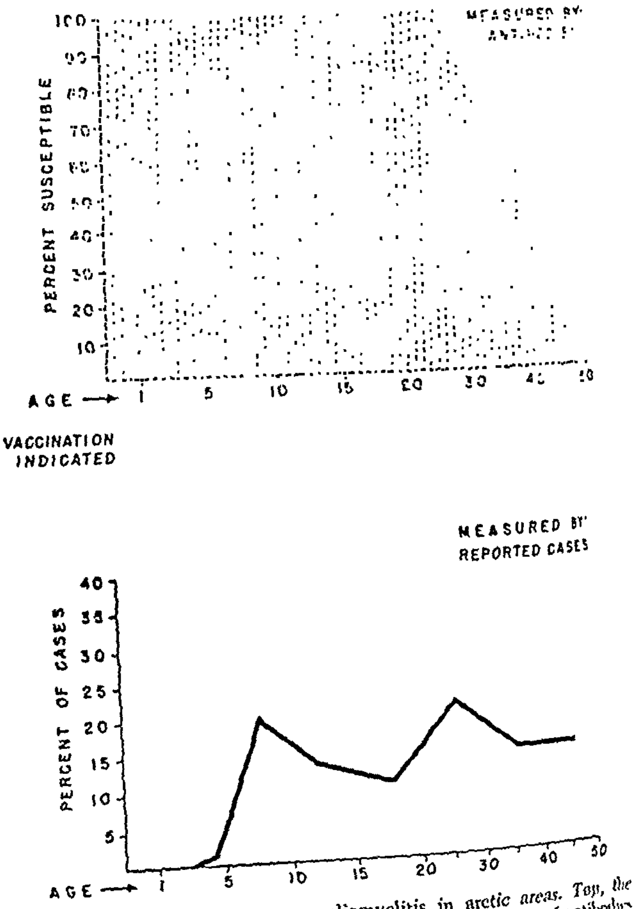

Fig. 2.—Status of immunity to poliomyelitis in arctic areas. *Top*, the period of susceptibility (vertical lines) as measured by a lack of antibodies to type 1 poliovirus. *Bottom*, the age distribution of cases in two of the rare arctic epidemics.

The status of immunity against poliomyelitis in a remote arctic population as estimated from series of clinical cases, and a serologic survey[6] is depicted in figure 2. What would be the routine indications for vaccination in an arctic population of this type? For the first antipoliomyelitis vaccination program to be carried out in such a population, probably everyone within the community should be vaccinated, old as well as young. Subsequently, owing to the infrequency with which polioviruses enter the community, it is possible that artificial vaccination of some kind might well be repeated in these areas every few years, if immunity is to be maintained. Decisions here might be aided by sequential antibody surveys.

To turn next to the opposite situation of the "immune population," such as is seen in populations in the Middle East[7] or North Africa,[8] or in others with comparable primitive living conditions, solid immunity comes early and 90% of the paralytic disease that does occur can be found in children under 5 years of age—the old-fashioned infantile paralysis (fig. 3). Serologic evidence through the use of the complement-fixation test also indicates that inapparent infections capable of inducing complement-fixing antibodies virtually cease soon after this age. This stands in great contrast to the situation in most parts of the United States as well as in the Arctic. There would be little need today to vaccinate children in North Africa or the Middle East, unless one restricted the priority group to the youngest children, representing those of the age group of 7 months to 3 or 4 years.

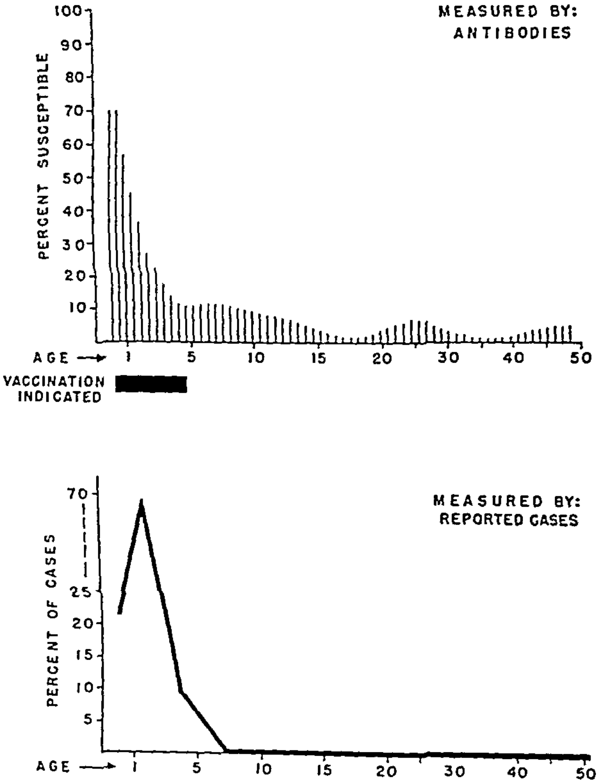

Fig 3 —Status of immunity to poliomyelitis in North African populations The percentage of adults without antibodies in such populations is small (*upper panel*), and when paralytic cases occur they are virtually confined to the youngest age groups

In the United States, there are all gradations of susceptibility and immunity. Not only do the poliomyelitis incidence rates vary geographically between northeastern, north central, and southern areas of the United States but the age distribution of acute paralytic cases within these regions also differs somewhat. Differences in the latter may exist between white and nonwhite populations. In some areas, such as the Latin-American population of three counties in southern Texas, there is a situation almost like North Africa and the Middle East[9]; in others, which represent some of our "best" areas, it is almost frighteningly like the Arctic.[10] The differences in the age distribution of poliomyelitis cases between these areas, surveyed more or less simultaneously (1948-1954), are as great as those separated in time by 40 years in Connecticut: the Hidalgo County, Texas, age distribution being similar to that of Connecticut in 1916, and others to that of 1955 (fig. 1).

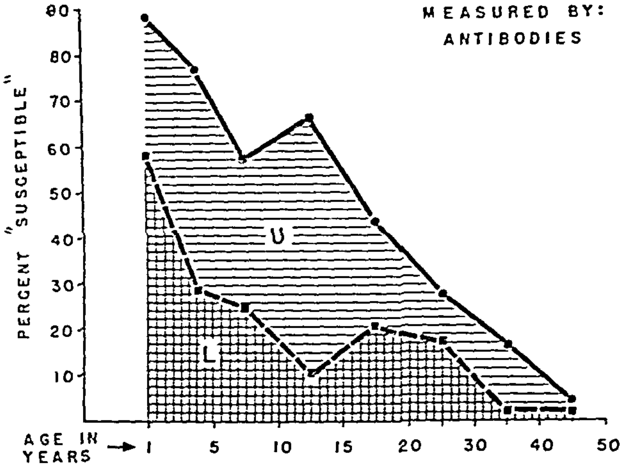

Fig 4 —Comparison of rates at which antibodies to poliomyelitis were acquired in two different socioeconomic groups, living in the same city, Charleston, W. Va U = upper socioeconomic group, L = lower socioeconomic group.

In the United States there are gradations within the same city. A population living in the poorest urban area acquires infection and gains its immunity to poliomyelitis early in life, that is in infancy; an urban or suburban population living in or near the same city, but in better quarters, acquires infection and gains its immunity later in life. Such intraurban observations have been carried out recently in Charleston, W. Va.[11] (fig. 4).

Antibody surveys, if done in the United States, should include the age groups from 18 to 30, for one of the disturbing features about the age incidence of paralytic poliomyelitis in this country today is the increasing frequency of adult cases, often in young parents. Young parents run the extra risk of being infected by their children, who may pick up the virus, perhaps in a nursery school, and as a result expose their parents, particularly their mothers,[12] to a heavier dosage of virus than the latter would ordinarily receive in the environment in which they live. The predominance of female cases in the group from 20 to 30 years of age may possibly be due to an increased susceptibility of pregnant women as well as to greater exposure. The increased rate of paralytic cases in this age group (fig. 1, 1955, and fig. 2), as well as the sex differences, demands more observation and study. Meanwhile indications for vaccinating young parents are appreciable.

instance even when all three types were fed simultaneously. However, a delay in appearance of antibody and titers in the lower range were observed in some of the men.

In the early stages of using a living attenuated poliovirus vaccine, it would be desirable to administer only one type at a time in order that one might have a better chance of identifying a paralytic disease due to spontaneous infection prior to ingestion of the vaccine. Accordingly, the feasibility of administering 100,000 ID of the optimum available attenuated strain of each type at three-week intervals was tested in 16 volunteers and found to be satisfactory. Although some of the volunteers stopped excreting one type of virus before the next type was fed, one pattern obtaining in those who were still excreting virus at the time of the next feeding is shown in figure 1. It can be seen that for a few days, occasionally as long as a week, both types of virus continued to be excreted before the new type became dominant.

Viremia.—In five to seven repeated tests for viremia on each of 50 chimpanzees and 72 human volunteers infected with various laboratory-developed attenuated strains of all three types, poliovirus was not demonstrated in a single instance during the preantibody phase of the infection. With several naturally occurring attenuated strains, transitory traces were occasionally found in the blood of both chimpanzees and human beings. These studies suggest that the viremia observed in nature and in champanzees and monkeys experimentally infected with virulent strains cannot be the result of viral multiplication in the alimentary tract and is probably due to multiplication elsewhere in the body.

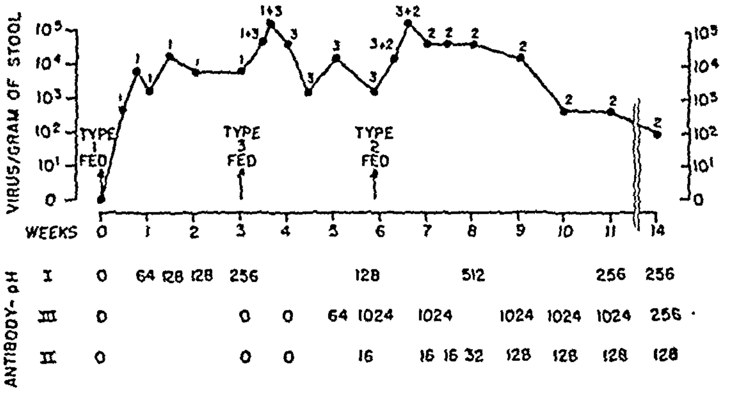

Fig. 1.—One pattern of virus multiplication in the human alimentary tract when 10^5 plaque-forming units of three immunologic types of attenuated poliovirus were fed at three-week intervals to an adult volunteer without antibody for any of three types of poliovirus. Numbers over dots indicate types of virus being excreted.

Antibody Development.—All alimentary infections have been associated with development of antibody, although the actual titers varied with the individual as well with the strain of virus. During the past year, Chanock and I found that neutralizing antibodies of different avidity appear at different times after natural infection with virulent strains, after experimental infection with attenuated strains, and after inoculation with formalinized vaccine. The antibody of low avidity, best demonstrable by the pH test, appears first and its titer can be more than 60 times higher than the antibody of high avidity demonstrated by the cytopathogenic test against 100 ID of virus in roller tubes. We have found a certain number of people with natural subclinical infections who have only the low-avidity antibody demonstrable by the pH test, and the same was also true of several volunteers infected with the type 1, L Sc strain or the type 3, attenuated Leon virus. Koprowski[2c] reported no significant change in titer of type 2 antibody in a group of 11 individuals 4½ to 5½ years after feeding of his original TN strain of reduced intracerebral virulence for monkeys. Our own tests on a group of 11 men one year after feeding one or another of three types of attenuated virus showed no significant change in the level of antibody, the low levels remaining low and the high levels remaining high.

TABLE 3.—*Effect of Feeding 10⁵ Plaque-Forming Units of Type 1 Attenuated Poliovirus (L Sc Strain) to Volunteers*

Group	No. of Volunteers	No. Who Excreted Virus	No. of Days Each Excreted Virus	Peak Virus Titers in Stool, Log₁₀ TCD₅₀*/Gm.
No antibody	11	11	10, 10, 10, 10, 21+†, 25+, 26+, 26+, 26+, 41, 77	3.7, 3.7, 3.7, 3.7, 3.7, 3.7, 4.2, 4.2, 4.2, 4.2, 4.2
Antibody after Salk vaccine	8	8	9, 10, 10, 13 14, 21+, 26+, 42	2.7, 3.2, 3.4, 3.7 4.2, 4.2, 4.7, 4.7
Naturally acquired antibody	8	1	10	4.2

* TCD₅₀, tissue culture dose₅₀.
† Volunteer fed another type of poliovirus and excretion of type 1 interfered with.

Multiplication of Virus in the Alimentary Tract in the Presence of Antibody Acquired in Different Ways.—Bodian's experimental studies on monkeys and chimpanzees have shown that the alimentary tract can be infected in the presence of certain levels of passively transmitted antibodies.[10] Koprowski and his associates[11] showed that the low levels of antibody passively transmitted by small doses of gamma globulin or the higher levels of placentally transmitted antibody in infants did not interfere with the multiplication of attenuated type 1 or type 2 poliovirus in the alimentary tract. Howe's studies on 19 chimpanzees extensively hyperimmunized with formalinized vaccine indicated that alimentary infection was reduced by about 50% after feeding of virulent type 1 virus,[12] but these studies cannot be transposed to humans, since in champanzees the throat is the dominant site for infection and the throat secretions are known to contain antibody when the serum antibody level is

TABLE 4.—*Lack of Relationship Between Titer of Preexisting Homotypic Antibody and Interference with Multiplication of Type 1 Poliovirus in Human Intestinal Tract*

Antibody After Salk Vaccine (2 Doses)				Naturally Acquired Antibody			
	Antibody Titer				Antibody Titer		
Volunteer No.	High Avidity Roller Tubes	Low Avidity pH Test	Duration of Excretion Days	Volunteer No.	High Avidity Roller Tubes	Low Avidity pH Test	Duration of Excretion Days
1	0?	16	26+?	1	0	4?	0
2	±	32	14	2	0	4	0
3	±	128	21+?	3	0	8	0
4	3	64	10	4	3	8	10
5	4	256	10	5	4	16	0
6	4+?	32	10	6	32	32	0
7	20	256	42	7	200	256	0
8	64	256	14	8	320	512	0

above a certain minimum. My own studies during the past year have shown a marked difference between the resistance of the alimentary tract to infection in those who have acquired their immunity by subclinical infection and those who developed antibody after two doses of Salk vaccine.

The data in table 3 show that neither the duration of virus excretion nor the peak virus titers per gram of stool were significantly different among the eight volunteers who were fed 100,000 ID of type 1 virus after two doses of Salk vaccine (the interval between the two doses was about four weeks, and the virus was fed two to three weeks after the second dose) and the 11 volunteers without antibody who were infected with the same dose of the same lot of virus. However, among eight volunteers with varying levels of naturally acquired antibody for all three types, there was no infection in seven. The data in table 4 show the lack of any relationship between the level of preexisting antibody, of low or high avidity, and the interference with viral multiplication in the lower alimentary tract. It is possible that the one naturally immune individual in whom the virus multiplied may not have had a previous type 1 infection, his very low level of type 1 antibody being the result of a group response to his type 2 or 3 infection. Similar results were obtained after feeding of type 2 and type 3 virus after two doses of Salk vaccine, but among the naturally immune controls virus multiplication also occurred in two of six fed the type 2 virus and in three of six who received the type 3 virus.

Reinfection tests on volunteers three months after experimental feeding of the type 3, attenuated Leon virus yielded similar results, and resistance of the alimentary tract to 1 million ID was observed in a volunteer who had only minimal amounts of low-avidity antibody. These results have a double significance. On the one hand they prove that subclinical infection can occur in those who have had formalinized vaccine and that it is possible to use a combination of the two types of vaccine, and on the other hand they indicate that a killed-virus vaccine alone may be expected to have little effect on the dissemination of polioviruses in nature. The latter conclusion is also supported by the observations of Lipson, Robbins, and Woods[13] and those of Gelfand and his associates[14] on the excretion of poliovirus under natural conditions of infection in children given Salk vaccine.

Neurotropism of Excreted Virus After Feeding of Various Attenuated Strains.—The most important question in these studies is whether attenuated viruses can become sufficiently more neurotropic after propagation in the alimentary tract to constitute a risk not only to the person who ingested the virus but to others to whom it might spread. It would be much easier to obtain the answer if we were dealing with an all or none property rather than with a spectrum of activity that can be measured only by quantitative tests in monkeys. Using extracts of the original stool, it is as a rule possible to inoculate only 100 to 10,000 ID, and a negative result indicates that the predominant virus population in the stool is attenuated to this extent, although here too paralysis of an occasional monkey may only reflect the capacity of the monkey nervous system to select a few more neurotropic particles from the larger inoculum. To permit more definitive tests, it has been necessary to increase the amount of virus by growing it in tissue culture before tests are made in monkeys.

TABLE 5.—*Screening of Thirteen Attenuated Strains of Poliovirus by Tests in Alimentary Tract of Chimpanzees and Men*

			No. Tested		Results of Alimentary Infection				
Type	Strain	Spinal Activity in Monkeys	Chimpanzees	Men	Antibody	Viremia	Alimentary Multiplication	Stability of Virus	Preference for Orally Given Vaccine
1	Brunhilde Enders	(High)†	4	...	+++	0	+++	Yes	No
	Mahoney-LSa mouse Cinci	Low	3	...	(0 to +)	0	—	Yes	No
	Mahoney KP 33	(High)	8	10	+++	0	++++	(No)	No
	Mahoney L Sc Cinci	Lowest	3	33	++	0	++	Yes	Yes'
	Cleveland 80-4*	Intermediate	3	—	+++	Slight	+++	(No)	No
	New Orleans P 1553*	Intermediate	3	—	+++	Slight	+++	(No)	No
	New Orleans P 2226*	Intermediate	—	6	++++	Slight	+++	(No)	No
	New Orleans P 2149*	Low	—	14	++++	Slight	+++	(No)	No
2	Y SK KP 51	*Intermediate*	14	14	+++	0	+++	(No)	No
	Cincinnati FAF 117*	(High)	3	—	+++	Slight	+++	(No)	No
	New Orleans P 712*	Low	—	38	+++	Trace rare	++++	Yes	Yes!
3	Leon KP 34 and 37	Low	8	44	++	0	++++	Yes	Yes'
	Cincinnati Glenn*	High	3	13	++	0	+++	Yes	No

* Naturally occurring strains

† Properties in parentheses eliminated strain

During the past four years, I have tested 40 chimpanzee and 68 human stools (in a number of instances several specimens from the same individuals) and the cultures derived from them for neurotropism in monkeys. The results were different with different strains, depending in part on how extensively attenuated the original virus was and how mixed the population that was fed. The results of these tests as well as those reported by Koprowski[2] in the tests he has carried out with his strains permit only the broad conclusion that reversion to high virulence has not been demonstrated and that the alimentary tract does not selectively favor more neurotropic poliovirus. Since the intestinal tract provides a large surface for viral propagation that can continue for many generations over a period of weeks, it is clear that the more mixed the original population and the more neurotropic the bulk of the viral population, the more frequently one may expect to encounter virus of greater neurotropism in the stools. This in fact occurred with the least attenuated Mahoney strain as well as with all of the naturally occurring type 1 attenuated viruses.

The indication that the alimentary tract does not selectively favor the more neurotropic particles was derived from observations that greater neurotropism of virus in the stools was a chance finding encountered in some and not in others, sometimes during the first two weeks and not later in the same individual and sometimes the reverse; i. e., *not in the early specimens* but in the later ones. In the one volunteer who excreted virus for 140 days after ingestion of the partly attenuated Mahoney strain, neither the original stool nor the culture fluid derived from it showed evidence of greater neurotropism at 140 days, although the 9-day stool specimen did. More highly neurotropic stool cultures that paralyzed monkeys after intracerebral inoculation of 10,000 ID were in three instances inoculated intraspinally in doses exceeding 1 million infective virus particles in nine chimpanzees without production of paralysis. Nevertheless, in selecting attenuated strains for further study, all those that even occasionally yielded stools or stool cultures that produced paralysis in intracerebrally inoculated monkeys at the 10,000 to 100,000 level were eliminated as being either too mixed or too neurotropic. Six of eight type 1 strains that I had tested in chimpanzess or in human volunteers or both (table 5) and Koprowski's type 1 (SM) strain [2] had to be eliminated on this basis, and only the most highly attenuated L Sc strain originally developed by Li and Schaeffer [8] and further purified in my laboratory proved to be satisfactory. The most suitable candidate for the type 2 strain was segregated from the stool of a healthy child that was sent to me by Drs. Fox and Gelfand of New Orleans and designated as P 712, and the type 3 strain that fulfilled these requirements was an attenuated derivative of the original Leon virus segregated in my laboratory.[3] The type 2 strains used by Koprowski and his associates [15] were eliminated chiefly because of their greater neurotropism.

TABLE 6.—*Isolation of Polioviruses with Varying Neurotropic Activity from Highly Attenuated Virus Populations Previously Purified by Terminal Dilution Technique*

Type and Strain	Material Tested		Paralysis in Cynomolgus Monkeys with No. of TCID* 1,000,000	100,000	10,000
3 Leon	Kidney passage 31		3/4	1/4	1/4
	36†		6/9	5/17	0/17
	Progeny of 9 triply purified plaques from kidney passage 31	Plaque 1†	0/29	0/14	0/11
		2†	0/15	0/15	0/15
		Plaques 3, 4, 5, 6	3/5 or 4/5	2/5 or 3/5	
		Plaques 7, 8, 9	4/5 or 5/5	5/5 or 4/5	
2 P 712	Kidney passage 4		2/4	0/8	0/4
	6†		6/17	5/17	4/17
	Progeny of 9 triply purified plaques from kidney passage 4	Plaque 1†	2 sl‡/21	0/19	1 sl/19
		Plaque 2	5/10	2/5	4/5
		3 to 9	3, 4 or 5/5	2, 3 or 4/5	
1 L Sc Cincinnati	Kidney passages 1 to 5†		4/20	0/8	0/10
	7†		5 sl/17	2/17	1/17
	Progeny of 10 triply purified plaques from kidney passage 5	Plaque 1†	3 tr§/15	0/15	0/10
		2	1 tr/10	2/10	1 tr/5
		3	1 sl/10	0/5	2/5
		4	0/10	2/5	3/5
		Plaques 5, 6, 7	1/5	2/5	
		8, 9	2 or 3/5	1 or 2/5	
		Plaque 10	3/5	3/5	

* TCID, tissue culture infective dose.
† Composite of tests on several different lots.
‡ sl, slight and limited involvement only.
§ tr, transitory questionable effect frequently associated with extensive traumatic lesion at site of inoculation.

Stability on Propagation in Large Lots.—The stability of these three selected strains on large-scale cultivation in monkey kidney was tested by preparing 20-liter lots of each. Various tests failed to reveal any simian cytopathogenic agents in these 60 liters of culture fluid. The intracerebral and intraspinal titrations in monkeys as well as the spinal tests in a total of 15 chimpanzees yielded results that were identical with those previously obtained with the seed lots. These lots were employed in 53 human volunteers, establishing among other things the effectiveness of 0.01 ml. of culture fluid (100,000 plaque-forming units) as a standard dose. Despite this demonstrated stability on large-scale cultivation, an analysis of a large number of individual virus particles, in the form of progeny from triply purified plaques, showed that the original seed viruses were not homogeneous and that still more highly attenuated viruses could be isolated.

Neurotropic Activity of Progeny of Individual Virus Particles Recovered from Optimum Attenuated Strains.—Data are summarized in table 6 concerning the neurotropic activity of the progeny of individual virus particles recovered from optimum attenuated strains. Reproducible spinal titrations in monkeys were obtained with cultures grown from the original type 3 seed virus in large or small amounts with virus inoculums of different size, but the progeny obtained from nine individuals particles yielded entirely different results. Three (plaques 7, 8, and 9) were distinctly more neurotropic, and four (plaques 3, 4, 5, and 6) were similar in activity to the parent population; two of the plaques yielded for the first time virus that in the largest doses was not paralytogenic in large numbers of monkeys. The results obtained with the type 2 virus showed a similar inhomogeneity, and the progeny from one of the nine plaques tested (plaque 1) was distinctly superior to all the others. Subsequent passages in cultures at a pH of 7.6 to 7.8 yielded virus that was nonparalytogenic in the largest doses. It should be pointed out here that these nonparalytogenic variants still have a certain minimal residual

TABLE 7.—*Influence of pH of Medium at Time of Inoculation on Yield of Infective Virulent and Attenuated Poliovirus Particles per Cell in Monkey-Kidney Cultures**

Type	Strain	Virulence for Monkeys	Hours for Necrosis of All Cells pH 6.8	pH 7.8	Yield of Virus PFU †/Ml. pH 6.8	pH 7.8	Infective Virus per Cell pH 6.8‡	pH 7.8§
2	YSK, KP_{10}	High intracerebral	38	38	2.6×10^7	7×10^7	350	70
	P 712, 10 ab_1	Lowest spinal	80	44	3×10^6	2.4×10^7	40	51
3	LEON, KP_3	High intracerebral	64	48	2.1×10^7	1.2×10^9	280	120
	LEON, 12 a_1b	None at 10^6 PFU spinal	96	48	3.2×10^6	3.2×10^7	43	331
	LEON, 14 ab	None at 10^6 PFU spinal	72	48	5.2×10^6	4.5×10^7	69	470

* 1 plaque-forming unit of virus added per 100 epithelial cells.
† PFU, plaque-forming unit.
‡ 150,000 cells present in control pH 6.8 roller tubes at time of beginning cytopathogenic effect.
§ 200,000 cells present in control pH 7.8 roller tubes at time of beginning cytopathogenic effect.

neurotropism, for, while some of the monkeys show no specific lesions of any kind even in the gray matter adjacent to the inoculum, focal poliomyelitis lesions are present in others. These new single-particle strains have been fed to 10 chimpanzees, and they produced immunogenic alimentary infections in all.

The type 1, L Sc strain, which already possessed such low activity that monkeys inoculated intraspinally with 1 million ID only irregularly exhibited slight localized, often only transitory, paralysis also revealed somewhat different patterns among the progeny derived from 10 different plaques. Particularly noteworthy was the fact that the progeny of some of the virus particles (especially plaques 3 and 4) exhibited the zone phenomenon, while others did not. The zone phenomenon [3c] is characterized by the appearance of paralysis in monkeys inoculated with smaller doses and not with larger ones. The progeny of plaque 1, devoid of this zone phenomenon, was distinctly superior to all the others. Similar tests in monkeys with the progeny of 14 plaques from the two optimum naturally occurring attenuated type 1 strains (P 2149 and P 2226) showed that all of them were highly paralytogenic intraspinally at both the 1 million and 100,000 dose levels. Still another attempt to obtain type 1 virus that might be superior to that derived from the best L Sc plaque was made by an analysis of four individual plaques derived from a culture of human stool obtained 15 days after ingestion of the original L Sc seed virus. This stool culture had the same low activity intraspinally in monkeys as the progeny of the best L Sc plaque and was also devoid of a zone phenomenon. The viruses recovered from these four plaques were similar in their activity to that of the parent culture but not superior to the best L Sc plaque.

Relationship between Plaque Size and Neurotropism.—A definite relationship between neurotropism and plaque size in vitro has been found for the type 3 and 2 but not for the type 1 viruses. Under the special conditions in the rubber-stoppered plaque bottles prepared by the technique of Hsiung and Melnick,[16] the smallest plaques were produced by the most highly attenuated strains. Figure 2 shows the sizes of plaques at the same time after inoculation of the original highly virulent type 3 Leon virus, of the attenuated derivative segregated from it after many passages in monkey-kidney cultures, and of the nonparalytogenic progeny of the two particles that were in turn segregated from it.

Relationship Between pH of Culture Medium and Yield of Virus by Virulent and Attenuated Strains.—During the course of our work with various attenuated strains, it was observed that the yield of virus was at least tenfold less when they were propagated in tissue cultures that had metabolized sufficiently to reduce the pH of the medium to 6.8 or less. Dulbecco and Vogt,[17] working with strains of known neurotropism from my laboratory, recently discovered a distinct relationship between neurotropism and plating efficiency on acid and alkaline plates. They found that, while the virulent viruses yielded as many plaques on the acid as on the alkaline plates, the more attenuated the strains were the fewer plaques they produced on the acid plates at a given time after inoculation. These differences (as high as one-million-fold) were most marked with our newly isolated single-plaque strains. Tests that I carried out (table 7) showed that, while with virulent strains the yield of infective virus per cell was only slightly greater at pH 7.8 (high bicarbonate reserve) than at pH 6.8 (low bicarbonate reserve), it was six-to-eight-fold less at pH 6.8 for the most highly attenuated single-plaque strains. This means that propagation at an acid pH would favor the more neurotropic mutants that might emerge, and conversely that propagation at an appropriate alkaline pH would prevent the enrichment of such mutants in the culture medium.

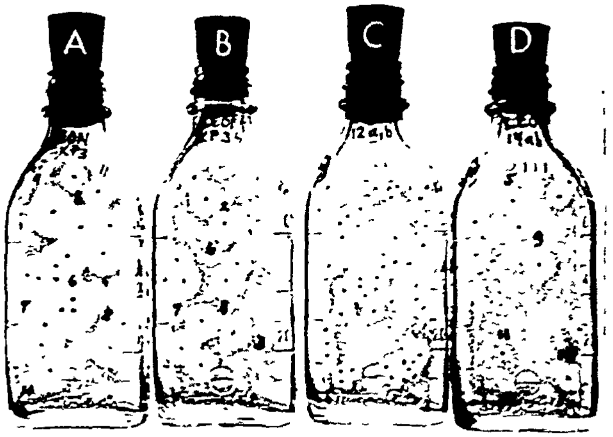

Fig. 2.—Relationship between size of plaques on a given day after inoculation and neurotropism in cynomolgus monkeys of virulent type 3 parent poliovirus and attenuated progeny segregated from it. All plaques were grown at the same time and photographed five days after inoculation. *A*, plaques highly virulent intracerebrally. *B*, inactive at 10^6-10^7 intracerebrally, intermediate activity intraspinally. *C* and *D*, purified plaque progeny isolated from Leon, KP_{34}. Not paralytogenic intraspinally in doses as high as 6 million plaque-forming units. Different size of plaques in same bottle may only reflect different day of first appearance.

Comment

It may be said that much has been learned about the basic principles underlying immunization with attenuated polioviruses by the oral route and that we now have strains derived from single particles of virus that are sufficiently highly attenuated and stable under appropriate conditions of cultivation to justify their use for the next stepwise studies on immunization of human beings. Experience has taught me the importance of accentuating the negative, and I therefore wish to stress that we are not ready for so-called mass trials of an orally given vaccine but only for those tests on increasingly larger groups that must precede any consideration of tests on a large scale. I also want to accentuate the positive by saying that the Salk vaccine is the only poliomyelitis vaccine available for public use at this time and that advantage should be taken of its protective effects to the maximum extent of its availability. I may add that some of my earlier reservations disappeared with the demonstration that the antibodies and immunity produced by the Salk vaccine do not interfere with the alimentary infection produced by an orally given attenuated vaccine or naturally acquired virus. This then is as far as we have gone, and it is obvious that we still have a great deal to learn before the ultimate goal of complete elimination of poliomyelitis is achieved.

Elland Avenue and Bethesda (29).

The following fellows-in-training and associates assisted in this study at different times and for different periods during the past four years: G. Berg, M. Bornstein, R. M. Chanock, V. Drouhet, H. Gerth, W. A. Hennessen, D. Laron, G. Lum, C. Moscovici, H. Nakai, M. Ramos-Alvarez, A. J. F. Schwarz, and S. S. Wang.

This study was aided by a grant from the National Foundation for Infantile Paralysis.

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CONSERVATIVE THERAPY IN PERIPHERAL NERVE DYSFUNCTION

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• *The mechanical properties of nerve fibers and the changes they undergo during and after mechanical strains are well understood. This knowledge affords a factual basis for the diagnosis and treatment of peripheral nerve dysfunction, as is illustrated by a detailed description of the physical therapy applied in a case of neuropathy of the facial nerve. The aim is to stimulate the contractile elements of muscle temporarily denervated, retain extensibility of fibrous tissues in and about the muscle, maintain elasticity of the capsule about affected joints, promote increased blood supply, and insure good position and motion of the affected part during the recovery period. Electrical stimulation, passive motion, assistive exercises, and dynamic bracing are important. Electromyography gives valuable information and can be used to motivate the patient. Exercise, to be effective, should be against sufficient resistance and should continue until the parts involved have regained strength in proportion to the demands of the patient's occupation.*

When a peripheral nerve is injured, it attempts to regenerate. The management of a peripheral nerve injury consists of providing the most favorable conditions for return of function. In commenting upon a paper by Perret in 1950, Loyal Davis[1] said, "More attention should be paid to keeping the muscles and joints in condition by all types of physical therapy and electrotherapy, so that, when the nerve does regenerate, the affected mechanism can work." Many factors cause peripheral nerve dysfunction, the most common being trauma; but anoxia[2] and infections such as herpes zoster[3] also occur. Assuming the etiology is known, management of the denervated motor elements and joints during the period of absent voluntary function must be based on pathophysiological conditions; thus, a review of some of these conditions is important.

Pathophysiology

According to the reaction of degeneration test, a denervated muscle fiber responds only to frequencies below 25 stimuli per second and chronaxy is lengthened; electromyographic studies show irregular spontaneous fibrillation potentials between 5 and 10 mv., which represent involuntary contractions by individual muscle fibers. No electrical potential is elicited by electromyography on attempted voluntary contraction in a denervated muscle. Studies of the gross muscle bulk during an extended period of denervation muscle atrophy show a loss of total substance.[4]

Chemical studies, particularly by Hines,[5] have indicated that this gross muscle atrophy indicates a reduction of the muscle-cell phase, in both absolute and

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Read before the Section on Physical Medicine at the 105th Annual Meeting of the American Medical Association, Chicago, June 13, 1956.

relative volume, whereas the non-muscle-cell phase undergoes an increase in relative volume, with no change in absolute volume. The chemical composition of atrophic muscle fibers is essentially the same as in the normal with respect to many constituents; however, certain substances such as glycogen show a decrease in concentration quite out of proportion to that attributed to mere reduction in volume. In his studies on the rat, Hines showed that in a normal muscle about 14% of chemical composition is attributed to the extracellular constituents and about 86% to the muscle cells. After 28 days of denervation in these rats, the total of chemical constituents is about 23% of the normal muscle, in which 50% of the chemical constituents comprise the muscle cells and 50% the non-muscle-cell substances.

Microscopic studies by Shaffer[4a] and his collaborators, Gutmann and Guttmann,[4b] and Adams, Denny-Brown, and Pearson[4c] demonstrate that, during muscle atrophy, fibers degenerate at irregular rates within a single muscle; there are areas of swelling of cytoplasm, cellular infiltration, vacuolation, and hyalinization. Bowden and Gutmann[6] found that irreversible dysfunction of muscles was associated with shrinkage of myofibers, relative increase of connective tissue, progressive depletion of cytoplasm at the motor end-plate, and progressive disturbance of vascularization. Thus, the muscle is in such a state after about three years that functional recovery will not occur despite reinnervation.

The effects of trauma to the nerve were studied by Denny-Brown[7] who reports that percussion of a nerve will produce a localized bulge associated with transient partial or complete paralysis and peripheral degeneration, according to the intensity of the blow. Regeneration tends to be rapid and complete. Kneading a nerve produces a severe intraneural hemorrhage that resolves rapidly until full function is restored. In a cat peroneal nerve, Denny-Brown demonstrated that a segment of this nerve could be stretched 100% of its length and that it exhibited a plastic effect, wherein the nerve tended to remain in the elongated position. Further stretch of the nerve caused petechial perineural hemorrhages, neural edema, dilated veins, and fibrosed and thrombosed arterioles. With violent stretching, the neurilemma tended to split longitudinally, producing herniation of fiber material; finally, with maximum traction, the neurilemma and its contents frayed into complete loss of continuity. He observed further that large nerves like the sciatic would not stretch as much as smaller nerve divisions, there being an inverse relationship between nerve diameter and elasticity.

In his studies on nerve repair, Hoen[8] reports, "A poor vascular bed for repaired nerve fosters the development of fibrous tissue." Further observation was made by Hoen relative to technical problems in joint motion and stretch of nerves across joints.[4d] Hoen agrees with Denny-Brown in that the central portion of a severed nerve that has normal structure and normal blood supply may be stretched under gentle and prolonged traction because it has normal ability to withstand stress and strain. It is further interesting to note from Hoen's studies that, in those cases wherein the distal section of a nerve stump had been inadvertently sutured to a central tendon, the constant traction on these nerve stumps caused complete fibrosis of the entire distal section of the nerve.

With respect to electrical stimulation, the literature is replete with scientific data compiled to justify[9] and refute[10] its efficacy. Most investigators of the effects of electrical stimulation on peripheral nerve damage concentrated their attention on muscle tension, while Wakim[9c] introduced the significant fact that blood flow is increased by electrical stimulation but bears no relationship to the characteristics of the current used. Nevertheless, from the studies of Bowden and Gutmann,[6] Osborne,[9d] Gutmann and Guttmann,[4b] and Shaffer and his co-workers,[4a] it can be concluded that muscle atrophy can be retarded by electrical stimulation providing (1) therapy begins early, (2) treatment is performed at frequent intervals, and (3) muscles under stimulation contract against resistance.

Having the benefit of such pathophysiological studies, the attending physician approaches the management of a case of peripheral nerve dysfunction by determining (1) etiology, (2) extent of injury, (3) appropriate specific surgical or chemical therapy, and (4) appropriate physical therapeutic measures to maintain optimum physiology of the affected part.

Therapy

Physical therapeutic measures are conservative in application but dynamic in effect, for they (1) stimulate the contractile elements of muscle during denervation, (2) retain extensibility of fibrous tissues surrounding each muscle fiber and fasciculus of fibers, (3) maintain elasticity of the capsule about affected joint, (4) promote increased blood supply, and (5) provide functional alignment and partial usage of the affected part during the denervation and recovery period.

The application of specific techniques of conservative therapy for neuropathy of the facial nerve (Bell's palsy) and for involvement of the nerve in an extremity is discussed below. It is assumed that the correct etiology has been established and proper surgical and/or drug management followed.

Neuropathy of Facial Nerve.—In neuropathy of the facial nerve, the patient is advised to keep the face warm by giving himself mild heat treatments for 15 minutes three times daily. If he goes outdoors in wind or cold temperature, he should protect the side of the face involved by a scarf or collar. He is also instructed to rinse his mouth after each meal and to rinse the eye on the affected side with isotonic sodium chloride solution twice daily or after exposure to air dust when out of doors. At these times, a patch over the eye is advisable. He is instructed to place a strip of cellophane tape, or adhesive tape, on the affected side of the face from the corner of the mouth to just in front of the ear. He begins by putting the tape on at the corner of the mouth, pulling the mouth upward and wrinkling the cheek, and fastening the other end of the tape in front of the ear. This pressure keeps food from getting lodged in the cheek and also minimizes the drooling of liquid out of the corner of the mouth on the affected side. Furthermore, such functional splinting prevents stretching of these small, denervated facial muscles that, being subjected to gravity forces, allow a sagging of the cheek and corner of the mouth.

Electrical stimulation by galvanic current is then prescribed. A voltage that produces the maximal muscle contraction tolerable is therapeutic, because it provides optimum summation of muscle fibers. The side of the face that is to be stimulated is generally preheated for 10 or 15 minutes with a mild infrared or radiant heat lamp. This reduces skin resistance and permits use of less voltage to obtain the same contraction. I prefer a surging, or sinusoidal-type, galvanic current at a rate of 20 stimuli per minute, which allows a rhythmical muscle response with each stimulus. Daily treatments of 15 to 30 minutes' duration are initially prescribed. In children under 12 years of age, electrical stimulation is not satisfactory because the voltage tolerated by the child is of so slight a magnitude that contraction seldom results. Fortunately, the period of motor dysfunction in neuropathy of the facial nerve in children is relatively short.

As one proceeds in therapy, faradic current is tried periodically to ascertain the first evidences of reinnervation. A response to faradic current is heralded by the observation that less galvanic current is required to give the same magnitude of contraction as originally necessary in the treatment. An alternating, or faradic, current of 200 to 1,000 impulses per second may eventually be used and will, in many instances, be more comfortable for the patient. Electrical stimulation is reduced in frequency with the advent of reinnervation. As traces of voluntary movement appear, the patient can exercise his own facial muscles; the frequency of supervised treatment, therefore, is reduced to once or twice weekly until it is felt maximum return of function has been achieved or is imminent.

Peripheral Nerve Dysfunction in an Extremity.—In treatment of peripheral nerve dysfunction in an extremity, the prescription calls initially for passive motion of the joints affected by the nerve dysfunction in order to maintain elasticity of the periarticular structures. This is gently carried out through full range and in all directions of joint movement.

Dynamic bracing to permit as much normal function as feasible has been well described by Von Wersowetz and co-workers,[11] Shields and Smith,[12] and many others. Dynamic bracing, as opposed to static splinting, offers the following benefits: It (1) retains a functioning extremity; (2) maintains circulation in the extremity through muscle action; (3) permits partial joint motion; and (4) permits involved muscles to be lengthened and contracted passively or assistively, as nonaffected muscles perform their normal function.

Electrical stimulation of denervated muscles is prescribed in the same general manner as described for neuropathy of the facial nerve. Though artificial, it is presently the only method available therapeutically for reproducing controlled muscle shortening in the absence of nerve supply. In an extremity it is advisable to use a voltage that gives maximum contractile response in the stimulated muscle and visible movement at the joint across which the affected muscle acts. Contraction against the resistance of 2-to-5-lb. weighted sandbags will provide a greater recruitment of muscle fiber. Osborne,[9a] presented data indicating that atrophy occurring prior to onset of electrical stimulation was not reversed.

As increasing motor units within a muscle are reinnervated, supportive aids such as electrical stimulation and passive motion are supplanted by assistive exercises. In my experience, inserting needles from the electromyograph into partially denervated muscles helps the patient exercise those fibers that will voluntarily respond. The wave frequency and height of oscillations on the oscilloscope give him visual evidence of muscle activity. The crackling of the loud-speaker adds auditory evidence. With additional motor units brought into action by increased effort, more waves occur on the oscilloscope; the sound of muscle contraction over the loud-speaker resembles that of a mechanical motor. The motivational effect on men and boys, especially, is profound. Electrical stimulation may be continued occasionally during this transition period until the part can be moved actively on the powder board. Progressive increments of weights used add friction, thus demanding maximum response from existing motor units.

Exercise with graduated resistance against gravity continues the process of demanding maximum response from active motor units as more muscle fibers are reinnervated. Exercises are continued until optimum strength and coordination are obtained, depending upon requirements of the involved parts in relation to the patient's employment. For instance, the serratus anterior of a plasterer requires more strengthening than that of a cashier. It is important, therefore, to pursue therapy until the muscle requirements of the patient's job are met.

Summary

Conservative therapy in peripheral nerve dysfunction is auxiliary in character but promotes optimum circulation, contractility, and elasticity of motor elements and minimizes secondary pathology associated with joint immobility and intramuscular fibrosis during the denervation period.

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SUBTOTAL GASTRECTOMY WITH AND WITHOUT VAGOTOMY FOR DUODENAL AND GASTROJEJUNAL ULCER

PRESENT STATUS

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• ***Subtotal gastrectomy alone was done in 224 patients and combined with infradiaphragmatic vagotomy in 217 patients who had duodenal and gastrojejunal ulcer. Of the three operative deaths, two were in the latter group but could not be ascribed to the vagotomy. Of the 17 proved instances of recurrent peptic ulcer disease, only one was in the vagotomized group. Vagotomy entailed an increase in postoperative morbidity and a risk of prolonged moderate diarrhea, but it afforded some protection against subsequent jejunal ulceration.***

Gastroenterostomy was done in 101 patients, with vagotomy in 70 of these. The rate of recurrences was 15% in the patients without and 10% in the patients with the vagotomy. It appeared that vagotomy afforded little protection to the patients with gastroenterostomy. A continuation of the subtotal gastrectomy of the Billroth 2 type, preferably combined with vagotomy, is recommended on the basis of this experience.

During the past decade, there appears to have been less reluctance on the part of the general practitioner and gastroenterologist to advise surgery for patients suffering from the complications of chronic duodenal ulceration. Many intelligent patients, becoming cognizant of the recurrent nature of the disease and its impact upon their social and economic life, are demanding operation. This change in attitude has not been fortuitous. The profession undoubtedly has been influenced by the lowered morbidity and mortality and the excellent results of gastric resection, and some sufferers from peptic ulcer have been swayed probably by the publicity accorded the "nerve operation," which for a time was a recurrent theme in the daily press. That there has been a renewal of interest in vagotomy as a complementary procedure in both gastroenterostomy and subtotal gastrectomy and as a supplementary one in the alleviation of gastrojejunal ulcer is quite apparent from the plethora of articles appearing in most medical journals.

This communication is concerned with (1) a few technical considerations that I believe to have been responsible for the lowered mortality and morbidity of subtotal gastrectomy, (2) the present status of this procedure with and without complementary vagotomy, and, briefly, (3) the effect of supplementary vagotomy upon gastrojejunal ulceration.

Operative Technique and Surgical Indications

For the past 30 years, I have considered subtotal gastrectomy of the Billroth 2 type the procedure of choice in the treatment of chronic duodenal ulcer. The operative technique at present is basically the one developed by the late A. A. Berg and R. Lewisohn, in which two-thirds to three-quarters of the stomach is removed, with gastrointestinal continuity restored by terminolateral gastrojejunostomy of the Hofmeister type. However, during the years my associates and I have made many changes, both in technique and in clinical approach, all designed primarily to lessen postoperative morbidity and mortality.[1] The improvements in anesthesiology and in preoperative and postoperative care, especially the correction of electrolyte imbalances, the maintenance of blood volume, and the use of antibiotics, need no comment.

The greatest hazard of subtotal gastrectomy of the Billroth 2 type is still the possibility of perforation of the duodenal stump with the development of fatal peritonitis. Many of these accidents can be prevented or their seriousness diminished by certain simple prophylactic precautions. In penetrating ulcers of the posterior wall or those situated in the second portion of the duodenum, removal of the lesion may entail injury to the common bile duct, the head of the pancreas, or the accessory pancreatic duct (duct of Santorini), leading to grave postoperative complications. This type of lesion should therefore be left alone. Removal of the ulcer is not an essential part of the operation as long as the pylorus and antrum have been completely resected. An ulcer left in situ is rarely the cause of immediate postoperative complications, and, moreover, it bears no relationship to the occurrence of subsequent gastrojejunal ulceration; in the majority of the patients in this series who developed subsequent gastrojejunal ulceration, the original ulcer by chance

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Read before the Section of Surgery, General and Abdominal, at the 105th Annual Meeting of the American Medical Association, Chicago, June 12, 1956 had been completely or partially removed. If the closure of the transected duodenum has been attended with difficulty and if there is an iota of doubt as to the security of the suture line, the area should be adequately drained, preferably through a right subcostal stab wound. In addition, the duodenum should be decompressed by the passage of a gastric tube through the gastroenteric stoma well into the afferent jejunal loop. I have never found it necessary to substitute a duodenostomy for a complete closure of the duodenum. (Personally, I would rather close a duodenum completely and anticipate the possibility of a duodenal fistula with a sump drain to which continuous suction could be applied, if necessary, than create one at the time of operation.)

Since 1937, gastrointestinal continuity has been restored routinely by an antecolic anastomosis of the Hofmeister type, with use of a short efferent jejunal loop. In addition to being perfectly satisfactory, this method is technically easier and has eliminated the danger of injury to the middle colic artery and the possibility of obstruction due to a prolapse of intestinal loops into the lesser omental sac, two possible complications in the performance of a posterior retrocolic gastrojejunostomy. Moreover, the separation of the anastomosis in the event of gastrojejunal ulceration presents few difficulties.

TABLE 1.—*Operative Mortality in 542 Patients*

Operation	Patients, No.		Deaths No.	Deaths %
Gastroenterostomy	28	101	5	5
Gastroenterostomy and vagotomy	73			
Subtotal gastrectomy	224		1	0.4
Subtotal gastrectomy and vagotomy	217		2	0.9

During the course of years, I also altered my clinical and surgical approach to several problems. It soon became apparent that hospitalized patients recuperating from the effects of a severe hemorrhage should never be operated on within a short time after their hemoglobin level and red blood cell count had been restored to normal; when they were, the operative mortality was considerable. These patients are now discharged for convalescent care for a period of at least six weeks, after which elective surgery may be performed with a minimal risk. Massive hemorrhages from a proved duodenal ulcer are rarely treated as surgical emergencies. Bleeding in most of these cases will cease spontaneously. If, however, after adequate blood replacement during a period of 24 to 36 hours, blood is lost as rapidly as it is transfused, immediate operation is indicated, as it also is in patients who apparently have stopped bleeding for a few days and then suddenly begin to hemorrhage again.

It was soon realized that not all patients would tolerate the magnitude of a gastric resection. If the operative mortality is to be kept at about 1%, a lesser surgical procedure must be substituted in selected cases. Gastroenterostomy, in spite of valid objections to it, was performed in about 18% of cases from 1946 to 1952.[2] It was used in 12 patients to evaluate the procedure. The remainder consisted of patients over 60 years of age who appeared physiologically older; those with severe diabetes; with chronic and advanced cardiovascular, pulmonary, nephritic, hepatic, or neurological diseases; and those who were extremely obese. Gastroenterostomy was also performed in patients in whom extensive edema and massive local infiltration would make a resection extremely difficult technically. Many experienced surgeons do not consider it a blow to their ego or a surrender of their technical ability or facility if a gastric resection is not performed because of severe systemic disease or local contraindications.

There were five deaths in this series of 101 patients undergoing gastroenterostomy. In 70, a complementary infradiaphragmatic vagotomy was performed. This high mortality for a simple procedure confirms the preoperative opinion that some of these patients probably would not have withstood the added trauma of a gastric resection. That I often made mistakes in judging the ability of patients to tolerate a major procedure is also true, because three in this group subsequently survived a subtotal gastrectomy for gastrojejunal ulcer.

Perhaps I have been a little too conservative in my surgery. I was probably lulled into a false sense of security by the hope that the addition of a vagotomy to a gastroenterostomy would materially lessen the incidence of gastrojejunal ulceration. I, as well as others, have been sadly disillusioned in this regard. In my experience, a small one to be sure, there has been to date a recurrence rate of 10% in patients with gastroenterostomy with a complementary vagotomy and 15% in those with gastroenterostomy alone. Yet some surgeons, whose results are obviously better, routinely choose gastroenterostomy and vagotomy for all patients with duodenal ulcer, reserving subtotal gastrectomy for those who subsequently develop gastrojejunal ulcer. However, I agree with those who feel that gastroenterostomy with vagotomy is indicated only in the poor-risk patients or when local conditions demand a conservative approach. In these instances it would appear illogical to employ the more hazardous operation of resection simply to improve upon the 85% expectancy of a good result with gastroenterostomy (preferably with vagotomy) if the patient survives.

Subtotal Gastrectomy With and Without Vagotomy

During the same period, 1946 through 1952, in which 101 patients were treated by gastroenterostomy, with or without vagotomy, subtotal gastrectomy of the Billroth 2 type was performed in 441 patients with chronic duodenal ulcer (table 1).

This procedure has always had its critics. They have stated that, in the hands of the average surgeon, the mortality is high and the end-results do not justify the magnitude of the procedure. These statements have been repeatedly refuted by the published records of many clinics. It is true, however, that in a small percentage of patients results are unsatisfactory. Some are rendered temporarily uncomfortable, others fail to gain weight due to nutritional disturbances, and a few are troubled by the dumping syndrome or diarrhea. A certain number will develop gastrojejunal ulceration. This latter complication, which is distressing and serious, has been reported in from 3 to 9% of the cases and often occurred in spite of the fact that the gastric resection was adequate and correctly performed. In these cases, high levels of free hydrochloric acid are usually present in the gastric aspirate. It became evident early in the experience of this clinic that the suppression of the chemical or hormonal phase of gastric secretion by resection did not always protect the patient against gastrojejunal ulceration.

TABLE 2.—*Length of Follow-Up of 390 Patients*

Yr. Followed	Patients, No. Subtotal Gastrectomy	Patients, No. Subtotal Gastrectomy with Vagotomy
9	3	1
8	5	5
7	15	9
6	15	11
5	34	19
4	27	48
3	34	17
2	37	35
1	36	39
Total	206	184

As early as 1927, Klein[7] conceived the idea of combining gastric resection with partial vagotomy in order to eliminate a second pathway to acid production, *i. e.*, psychic stimulation. With this combined method, he hoped to increase the incidence of achlorhydria, for, "no free acid, no ulcer." Subsequently, the follow-up results in 34 selected patients with high preoperative acidity in whom subtotal gastrectomy was combined with partial division of the vagus fibers on the anterior wall of the stomach seemed to verify Klein's contention.[4] In 1946, after the renewal of general interest in vagotomy as a definitive and sole procedure in the treatment of duodenal ulcer, I decided to combine subtotal gastrectomy with bilateral infradiaphragmatic vagotomy, provided the operative mortality and postoperative morbidity were not appreciably altered. At first, this combined procedure seemed especially indicated in the patients with duodenal ulcer in whom bleeding was the predominant symptom and those in whom preoperative acid levels were unusually high, two types of patients in whom jejunal erosions and ulcerations are most apt to occur. Subsequently, the indications were broadened, and, at present, the combined procedure is preferred whenever possible. However, in none of these cases has the extent of resection been lessened. I am not performing hemigastrectomy as yet.

The immediate postoperative results in 224 patients undergoing subtotal gastrectomy alone (group 1) and 217 undergoing the combined procedures of subtotal gastrectomy and infradiaphragmatic vagotomy (group 2) have been analyzed in detail in previous communications.[5] It may be stated briefly here that, postoperatively, there was a greater incidence of pulmonary complications, gastric retention, and vomiting and diarrhea after the combined procedure, but none of these proved serious. Three of the 441 patients died, one of them in group 1 and two in group 2, but none of these deaths was related to the vagotomy. Postmortem examinations revealed pancreatitis and bronchopneumonia in one, a massive pulmonary embolus (occurring on the second postoperative day) in the second, and necrosis of the body and tail of the pancreas in the third patient, who died on the 42nd postoperative day.

Follow-up of the patients in this series now covers one to nine years (table 2). During this period, there were seven deaths in group 1: one after 3 months due to a secondary resection for gastrojejunal ulcer; one after 10 months from an unknown cause; one after three years from carcinoma of the lung; three after four, five, and six years, respectively, from uremia; and one after seven years from a metastatic carcinoma of the brain. In group 2, there were four deaths: one after four months from homologous serum jaundice; one after six months from internal injuries incurred in an automobile accident; one from coronary thrombosis after a year; and one from cerebral hemorrhage after four years.

Follow-Up Results

The follow-up results have been classified as satisfactory or unsatisfactory, as judged by both the examiner and the patient (table 3). There are two types of patients with satisfactory results, the well and the improved. The former group includes patients who were well at all times after operation as well as those who had symptoms during convalescence or earlier follow-up but who were asymptomatic at the time of their last visit. The patients considered improved are those whose ulcer disease is apparently cured but who do have minor distressing symptoms. The unsatisfactory cases are those in which there have been proved jejunal ulcers or in which such lesions have been suspected. An "unclassified" group consists of those patients with symptoms and disturbances of gastrointestinal function sufficiently severe that the result can be labeled unsatisfactory but with no subjective or objective evidence of recurrent ulcer disease. There were two such patients in group 1 and three in group 2. All five suffered pain of moderate severity as well as either diarrhea, vomiting, or a mild dumping syndrome. Repeated careful examinations and x-ray studies failed to disclose the cause of these symptoms. One of these patients had a severe psychoneurosis.

TABLE 3.—*Results of Follow-Up of 390 Patients*

Results	Subtotal Gastrectomy No.		Subtotal Gastrectomy %		Subtotal Gastrectomy with Vagotomy No.		Subtotal Gastrectomy with Vagotomy %	
Satisfactory		184		90		179		97
Well	171		83		156		85	
Improved	13		7		23		12	
Unsatisfactory		21		10		5		3
Gastrojejunal ulcer	16		7.7		1		0.5	
Suspected ulcer	3				0			
Unclassified	2				4			

In group 1, of the 206 patients followed, results are satisfactory in 184 (90%) and unsatisfactory in 21 (10%). Of the patients with unsatisfactory results, 16 have had proved recurrences and 3 have had suspected recurrences, without hemorrhage, manifested by pain in one and a mild melena reported by the patient in 2. X-ray examinations in these patients were negative. There were two patients with side-effects, manifested by pain. In group 2, of the 184 patients followed, 179 (97%) are well, while of the 5 patients with unsatisfactory results, one has had a proved recurrence and 4 have had side-effects. One of these patients has a persistent and incapacitating diarrhea, and in the other four abdominal pain is present but the x-ray examinations are negative. Of the patients with results classified as satisfactory, six in group 1 and nine in group 2 had experienced a mild dumping syndrome. It may be surprising that we have observed no patient in whom there was a persistent and severe dumping syndrome, manifested by tachycardia, weakness, flushing, and fulness after meals. Many patients noticed an intolerance to milk and sweet drinks, but by eliminating these from their diets they were able to control their postcibal symptoms.

In the patients with proved recurrent peptic ulcer disease (16 in the group undergoing gastrectomy and one in the group undergoing gastrectomy and vagotomy), the presence of the ulcer was proved by either operation or x-ray examination or else was strongly suggested by massive gastrointestinal hemorrhage. Such bleeding may occasionally be the result of peristomal gastritis, erosions, or jejunitis, but it is most frequently due to actual jejunal ulceration. In any case, the operation that does not protect the patient from massive hemorrhage must be considered a failure. In this series, it has been considered evidence of recurrent ulceration and hence of an unsatisfactory result. The results in the patients undergoing gastrectomy alone are in very marked contrast to those in patients undergoing both gastrectomy and vagotomy, in whom, up to the time of writing, there has been but one recurrence. This occurred in a patient in whom, at the age of 18, a very high subtotal resection was done. Four years later, in 1952, a huge gastrojejunal ulcer developed that necessitated a total gastrectomy. When seen in 1955, the patient was well, without any side-effects.

A comparison of the results of the postoperative test meals showed that, regardless of the contents of the test meal or the time interval after operation, gastrectomy with complementary vagotomy consistently produced a higher percentage of patients with gastric anacidity than did gastrectomy alone. It would appear from these results that complementary vagotomy performed with subtotal gastrectomy in the surgical treatment of duodenal ulcer afforded added protection against recurrent disease at the cost of an increase in the postoperative morbidity and of a prolonged moderate diarrhea in about 10% of the cases; however, in only one patient was this diarrhea incapacitating. There is an impression that the undesirable side-effects of vagotomy do not justify its use and, moreover, that vagotomy should be reserved for the small percentage of patients in whom recurrent disease develops after gastrectomy. Twenty patients who developed gastrojejunal ulcer after subtotal gastroenterostomy were subsequently treated by supplemental vagotomy at this clinic; about 40% of the patients were not permanently benefited.[6] This simple procedure usually produced an immediate dramatic disappearance of the lesion, but ultimately the jejunal ulceration often recurred. It would seem that the best procedure in cases of gastrojejunal ulcer after a gastroenterostomy is not vagotomy alone but rather a high subtotal resection combined with vagotomy. Moreover, one should never expect vagotomy alone to be effective in treatment of a gastrojejunal ulcer occurring after subtotal gastrectomy if the previous resection has been inadequate or if the stoma has become obstructed. This type of case requires an additional resection, the correction of mechanical difficulty, or both.

There is also a group, fortunately small, of patients who have undergone subtotal gastrectomy in whom, regardless of the extent of the secondary gastric resection, even if combined with a complete vagotomy, unneutralized free acid is still secreted in large amounts and ulceration recurs. In the past, a total gastrectomy was the only effective remedy for this type of patient, and it was always performed reluctantly. I say "reluctantly" because most patients with total gastrectomy are not happy and suffer nutritional disturbances that require medical care throughout their life. Recently, Zollinger and Ellison[7] reported two instances of jejunal ulceration associated with hypersecretion and hyperacidity in which recurrent ulceration followed standard surgical therapy in both cases, finally necessitating a total gastrectomy. In each patient, nonspecific islet-cell tumors of the pancreas were eventually found. Certainly, in cases of this kind a careful search for individual tumors or even resection of the body and tail of the pancreas should be considered before a total gastrectomy is performed as a means of controlling secretion of free acid.

At the time of writing there is a wave of enthusiasm for revival of the Billroth 1 procedure, now often combined with vagotomy. Certain claims are made for its superiority because it has been stated that patients are able to maintain or gain weight, the incidence of the dumping syndrome is presumably lower, and there is, of course, no gastrojejunal ulceration. The latter is certainly true, but there are other possible complications, such as stenosis at the anastomosis and recurrence of duodenal ulcer. I shall reserve decision on the future usefulness of this procedure until subsequent follow-up statistics have been reported after an adequate period of observation.

Summary

As I reflect upon my experience over 30 years, I can state that, at present, results seem to justify a continuation of the subtotal gastrectomy of the Billroth 2 type, preferably combined with vagotomy. It is not a perfect procedure, but it has proved to be fairly satisfactory in my hands. The incidence of jejunal ulceration appeared lessened by the addition of complementary vagotomy at the cost of a slight increase in postoperative morbidity and in the incidence of a moderate diarrhea.

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Drs. Leonard J. Druckerman and Vernon A. Weinstein performed follow-up examinations of most patients in this series.

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MEDICAL EVALUATION OF THE BECK OPERATION FOR CORONARY ARTERY DISEASE

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• *The Beck operation, which consists of procedures to effect intercoronary blood-flow communications, has been performed on 185 patients in Cleveland. The operation relieves ischemic areas of the heart muscle, responsible for pain, and can prevent dangerous oxygen differentials that cause death; however, it cannot stop occlusive disease in the coronary arteries, nor restore degenerated myocardium. A positive diagnosis of coronary disease is the indication for operation (unless there is some specific contraindication), and the protection afforded by the operation need not be withheld until the patient has had at least one myocardial infarction. On 137 follow-up studies the long-term mortality has been reduced over one-half from what would be expected, and 90% of those patients still being followed have definite amelioration of previous symptoms. The low operative mortality is attested to by a series of 100 consecutive patients operated on, of which only one died prior to discharge from the hospital.*

The greatest single problem confronting the medical profession today is concerned with the catastrophic consequences of coronary artery disease. The occlusive degenerative process in the coronary arteries results in the incapacity of angina pectoris, the disability of myocardial infarction, and the disaster of the fatal heart attack. By its very nature, this process is progressive and eventually fatal. The annual death toll associated with coronary disease in the United States continues to increase and is fast approaching the half-million mark. This increase is not merely an expression of the general aging of the population; as a matter of fact, coronary disease has become increasingly common in the younger age groups. Many patients with definite coronary disease live out a normal life expectancy with little or no disability, but, unfortunately, the great majority are doomed to prolonged invalidism or sudden death. Despite the increasing devastation of this disease, there has developed a remarkable complacency and feeling of optimism toward the patient with coronary disease. This has progressed to the ridiculous rationalization that patients with coronary disease are better off than those who do not have the disease.

In a fundamental sense, angina pectoris, myocardial infarction, and cardiac arrest merely represent varying responses of the heart to the occlusive process in the coronary arteries. However, there *is no obligate relationship* between the degree of reduction in coronary inflow and the resulting consequences.[1] The essential role of intercoronary arterial channels in preventing the catastrophic consequences of coronary artery disease is evidence of the protection afforded by a more equal distribution of the available coronary inflow.[2] If this collateral circulation is adequate, complete occlusion of the coronary arteries may occur without significant muscle damage. The fate of the myocardium and, indeed, the fate of the patient depends upon the amount of blood available beyond the stenosis or occlusion of the coronary artery. The natural development of intercoronary communications is an uncertain process and is, unfortunately, most frequently inadequate.

Frequent electrocardiograms and the present medical optimism must not disguise the necessity for definitive treatment to provide an adequate distribution of blood to the myocardium. Some day, the occlusive process in the coronary arteries presumably will be reduced or prevented by medical means. However, for the present, the patient with coronary artery disease should have the benefit of any *treatment that is safe and effective.*

Surgical Treatment

The surgical treatment for coronary artery disease has been established on a firm scientific basis.[3] The principles and techniques developed by Beck are generally recognized and have stimulated many workers in this field. In a recent survey, I discovered that more than 50 thoracic surgeons in the United States (and at least 20 in Europe and Israel) have carried out the surgical treatment of coronary artery disease in well over 1,200 patients. The over-all operative and early postoperative mortality reported by these surgeons has ranged between 5 and 10%. Long-term follow-up studies have revealed complete or partial relief from symptoms in 80 to 90% of the patients evaluated. Despite certain variations in the surgical technique, the results have been remarkably similar.

This report is based on observations of 185 consecutive patients operated on in Cleveland by Beck since January, 1951. Briefly, the Beck operation consists of

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Read before the Section on General Practice at the 105th Annual Meeting of the American Medical Association, Chicago, June 13, 1956.

mechanical abrasion of the epicardium and parietal pericardium, partial ligation of the coronary sinus, instillation of powdered asbestos, and the application of mediastinal fat and pericardium to the heart. These procedures are effective in stimulating intercoronary communications and may bring added blood to the heart that has reduced coronary inflow. Effectiveness of the Beck operation has been demonstrated convincingly in the laboratory.[3] Test coronary artery ligation was followed by a much lower mortality rate in dogs that had had the Beck operation than in those not so protected, and resulting infarcts were smaller. Backflow measurements demonstrate increased blood supply beyond the occluded artery.

The clinical results in patients have confirmed the laboratory findings. However, in order to evaluate properly the surgical treatment of coronary disease, it is important to know not only what operation can do but also what it cannot do. It cannot stop the occlusive disease in the coronary arteries, nor can it restore degenerated myocardium. It can relieve ischemic areas responsible for pain; it can prevent dangerous oxygen differentials that cause death[4]; and it can prevent extensive infarction. It should be stressed that pain relief is achieved, not by interruption of pain pathways, but by overcoming the physiological derangement causing the pain. Obviously, interference with normal pain pathways, although possibly producing subjective relief, could not prolong life; on the contrary, such a procedure would result in earlier mortality. It will be shown that the Beck operation definitely increases life expectancy.

In properly selected patients, the mortality associated with operation has been remarkably low. As a matter of fact, in the last 62 consecutive patients operated on up to this time, the operative and early postoperative mortality has been zero. This signal achievement should remove the last imposing barrier to the surgical treatment of coronary artery disease.

Operability

Indications for Operation and Selection of Patients.—The diagnosis of coronary artery disease rests primarily on the patient's history. The electrocardiogram is merely confirmatory. In 25% of the patients in this series, the preoperative 12-lead electrocardiogram was within normal limits at rest. Exercise-tolerance tests, which were performed only in patients with normal control records, showed characteristic electrocardiographic changes of coronary insufficiency in one-half of these. The unreliability of the electrocardiogram was particularly evident in patients in whom serial electrocardiograms had always been normal. In 25% of such patients, exploration of the heart surface during operation, with the aid of exploratory direct epicardial electrograms, revealed previously undiagnosed infarcts.

A positive diagnosis of coronary disease is the indication for operation. The achievement of a low operative mortality rate now justifies the application of the operation to patients with very early disease, that is, before extensive myocardial damage has occurred. By the same token, the protection afforded by operation need not be withheld until the patient has had at least one myocardial infarction; early operation can reduce the 10 to 20% mortality rate associated with the first episode of myocardial infarction. Operation may also be performed even after several episodes of infarction, but, obviously, little benefit can be achieved if the heart has begun to dilate.

Classification of patients with coronary artery disease is particularly difficult. Consideration must be given not only to the degree of myocardial degeneration but also to the progression of the occlusive process in the arteries. The following preoperative classification has been found useful: Group 1 consists of patients, usually under 50 years of age, who have mild symptoms and who may have a small infarct and/or mild angina pectoris. Group 2 consists of patients with hearts of normal size who have moderate to severe angina pectoris; they may have one or more infarcts. Group 3 consists of the salvage cases—those patients with extensive muscle damage who may have an enlarged heart and congestive heart failure—as well as patients with status anginosus and those with certain contraindications for operation. The great majority of patients operated on are in group 2. However, the percentage of patients in group 1 is increasing. As a matter of fact, in members of families with a "bad" coronary history, operation should be considered at the earliest evidence of the disease.

Contraindications for Operation.—Acute myocardial infarction, or even suspicion of impending infarction, precludes operation for at least four to six months. In addition to the obvious dangers of operation during the acute stage, the delay allows for development of natural compensatory mechanisms. Operation is also hazardous in younger patients with rapidly progressive symptoms, particularly in those without previous myocardial infarction. These patients are prone to the development of areas of ischemia during or immediately after operation. Their hearts tend to develop electrical instability,[4] with resultant ventricular fibrillation, so that an impending medical death becomes a surgical mortality.

Cardiac enlargement and evidence of congestive failure constitute a relative contraindication to operation. However, in 20% of the patients operated on in this series, the left ventricle was fluoroscopically enlarged. At least one-fourth of these patients had objective evidence of early congestive failure. Although it is too late for much benefit in such patients, their hearts are remarkably stable and they tolerate operation quite well. Severe hypertension, or any other associated disease that in itself limits life expectancy, contraindicates operation. However, a moderate degree of blood pressure elevation was present in 25% of the patients operated on.

Significance of Age, Sex, and Duration of Symptoms.—In this series of 185 patients who were operated on, the age range was 27 to 72, with an average age of 48 years. Generally, patients over the age of 65 carry an increased operative risk, but operation is not denied such a patient if his tissue age justifies it.

Twenty patients in this series were over 60. In patients under 40 years of age, the rapidly progressive disease usually present in this age group tends to make operation somewhat hazardous. However, operation was carried out in 29 patients under 40 years of age. Less than 10% of the patients operated on were females.

In this series, 75% of the patients had suffered at least one clinically proved myocardial infarction. Two or more infarctions had occurred in 20%. Angina pectoris, ranging in severity from very mild to complete status anginosus, was present in 95% of the patients operated on. The duration of symptoms, in itself, of course gives no indication of the severity of the disease. The range of duration in this series was from four months to 13 years, with an average of 2.9 years. In general, patients with longer periods of duration of symptoms appeared to tolerate operation better.

Results

Mortality.—In the 185 patients operated on since January, 1951, there have been 11 deaths associated with surgery (2 during operation and 9 in the early postoperative period), for a total mortality rate of less than 6%. Careful selection of patients and improvements in medical and surgical management have resulted in a progressive lowering of operative mortality, as evidenced by the last 62 consecutive operations up to this time without a death. At least 15 of the 62 patients were salvage cases. However, in every instance symptoms had become fairly stable for a few months prior to operation. Recognition of the limitations of operation has prompted judicious delay in seriously ill patients. Certainly, if a castastrophe is imminent, an ill-timed operation will only hasten it. A delay of a few months permits time for stabilization and greatly enhances toleration of the operation and the achievement of a good result.

Evaluation.—Obviously, the very nature of the disease itself is such that there is no reliable objective method for the evaluation of any method of medical or surgical treatment for coronary artery disease. Reliance on the electrocardiogram or ballistocardiogram is indeed unrealistic. Furthermore, one must consider the fact that only a small alteration in previously compensated coronary circulation results in disability or death. By the same token, only a small amount of blood made available to a critical area can produce marked clinical benefit. Certainly, in the anginal attack, one would not question the immediate relief afforded by a tiny amount of glyceryl trinitrate merely because such a dramatic accomplishment may not be demonstrable electrocardiographically. Also, the remarkable and immediate response to glyceryl trinitrate further emphasizes the far-reaching effect of small alterations in coronary circulation.

Serial electrocardiograms and ballistocardiograms have been taken in most patients as part of their long-term evaluation. Significantly enough, in 40% of those having abnormal preoperative ballistocardiograms there has been evidence of improvement within the first year; however, there does not appear to be any obligate relationship between the degree of clinical improvement and that shown on the ballistocardiogram.[4a]

Generally speaking, each patient serves as his own control. No doubt, with a few more years of follow-up, a highly significant statistical evaluation will be forthcoming. For the present, evaluation of the effect of operation must rest upon the following factors: (1) increased life expectancy, (2) amelioration of symptoms, and (3) ability to work.

Long-term follow-up studies have been carried out on the 137 consecutive patients discharged over a period of six months to five years, with the average time since operation being two years. The expected mortality in such a group over this period would be 41, or 30%.[7] Actually, 18 are known or assumed to be dead, a mortality rate of 13.1%. Thus, even at this relatively early period, life expectancy can be shown to be increased by operation. Since operation does not prevent the occlusive process in the coronary arteries, a period of symptomatic improvement may be terminated by overwhelming occlusion and death. Such was the case in 50% of the patients who died six months to five years after operation.

Of the 100 consecutive patients who are alive and who could be evaluated over a six-month to five-year follow-up period, 45 are more or less completely free of pain. Another 45 claim considerable reduction in pain. Thus, 90% had a definite amelioration of symptoms. Only 10% had no observable improvement; however, evaluation in these was particularly difficult because of such complications as narcotic addiction, psychoses, and cerebrovascular accidents. Ability to work with no limitations was reported in 42 patients, while another 48 are better able to work, with some limitations. Thus, 90% are economically productive. Prior to the operation only 45% had been able to work half-time or more.

Summary and Conclusions

The Beck operation for coronary artery disease is a safe and effective procedure for providing a more adequate distribution of arterial blood to the heart. In the last 62 consecutive patients operated on, the mortality associated with operation has been zero. The over-all operative mortality since January, 1951, is less than 6%. Operation is indicated in patients with coronary artery disease unless there is a specific contraindication. The operation should not be considered as merely a salvage procedure; best results are achieved by operation early in the course of the disease. Long-term follow-up studies on patients who had undergone the Beck operation revealed a definite increase in life expectancy. Significant amelioration of symptoms occurred in 90% of the patients evaluated. Likewise, 90% of the patients were able to return to full-time or part-time work with less limitation.

Addendum

Since this paper was prepared, the series of consecutive patients operated on without immediate operative mortality has been extended to 100. The only death in this entire series occurred in a poor-risk patient who suffered an overwhelming coronary occlusion just prior to his anticipated discharge from the hospital.

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SPECIAL INDICATIONS FOR HYPNOSIS AS A METHOD OF ANESTHESIA

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• *The advantages of hypnosis as an alternative to conventional anesthesia in special instances are illustrated by accounts of five cases. In a pregnant woman about six weeks before term, the onset of poliomyelitis caused paralyses so extensive as to require tracheostomy and continuous respiratory assistance; when it was decided that labor should be induced, hypnosis was tried and found adequate for the delivery of a 2,664.9-gm. infant by low forceps. In a dental patient who had been insisting on general anesthesia after severe reactions to a local anesthetic, hypnosis solved the immediate problem and eventually diminished the patient's fear of dentistry. In a severe case of epilepsy, hypnosis sufficed for the craniotomy and excision of the epileptogenic focus in the temporal lobe after procaine was injected for the scalp incision. Hypnosis was found adequate similarly in a man who needed extensive débridement and grafting after thermal burns covering 45% of his body surface and in a girl who needed gynecologic surgery in the presence of severe congenital heart disease. The disadvantages of hypnosis, that it requires skill, is time-consuming, carries psychological risks, and fails in some subjects, are offset by its advantages in special cases. Its indiscriminate use .in uncomplicated cases is not recommended.*

The beginnings of the use of hypnosis as an analgesic agent go back to ancient times. One of the first recorded reports of its use in surgery in modern times is that of Esdaile, published in 1840. Since then there has been extensive documentation of its efficiency as an anesthetic agent. In spite of this, hypnosis has not yet gained widespread use as an anesthetic agent. This is due partly to the inherent difficulties in the hypnotic technique and to the quasi-scientific status that is usually associated with hypnotism in the mind of the scientific man. More important, however, than either of these is the rapid development of modern anesthesiology with its more efficient and safe techniques and chemical agents. Because of this, it hardly seems practical to advocate the general use of hypnosis as an anesthetic agent. It frequently happens, however, that special kinds of problems or procedures arise with patients in whom the administration of chemical anesthetics might be undesirable. For the past three years we have been investigating the use of hypnosis as a method of anesthesia in such special kinds of surgical problems. The purpose of this report is to present some of these problems and the results obtained through the use of hypnosis.

Report of Cases

Case 1.—A 32-year-old pregnant woman developed poliomyelitis about six weeks before term. Previously she had experienced three normal pregnancies and deliveries, and her fourth pregnancy had been completely normal prior to the onset of the poliomyelitis. Twenty-four hours after the patient's admission to the hospital, extensive paralysis occurred. Involvement of muscles of respiration limited her tidal volume to 200 ml. of air, as determined by pneumotachographic studies. Her vital capacity at this time was not significantly greater than her tidal volume, and control of pharyngeal secretions was accomplished with difficulty. A tracheotomy was performed, and her breathing was assisted by the use of an intermittent positive-pressure type of respirator. She needed continuous respiratory assistance, and it was elected to continue use of intermittent positive-pressure and nebulization with the patient in a comfortable low Fowler position.

Both the obstetrician and the respiratory consultant felt that emptying the uterus would improve the patient's general condition. Two days after the patient's admission, the obstetrician started an intravenous infusion of oxytocin injection (Pitocin) and isotonic sodium chloride solution. Excellent uterine contractions were maintained for about six hours, although dilatation of the cervix did not occur. Because the patient had become very tired and apprehensive, it was decided to delay further efforts at induction.

On the fourth day, the internist felt that delivery was more urgently indicated than ever in order to facilitate respiratory exchange. Consequently, another oxytocin infusion was started. This resulted in excellent uterine contractions. The membranes were ruptured, and labor progressed in a satisfactory way. During this prolonged period of labor, the patient had become increasingly anxious and apprehensive. Original plans to utilize a pudendal block to provide anesthesia for delivery were changed. Although use of an inhalation technique of anesthesia was not fundamentally ruled out, hypnosis was given consideration and one of us (H. B. C.) was consulted by the obstetrician concerning this method of anesthesia. The idea of using hypnosis was presented to the patient. Although she at first appeared resistant toward the method, rapport was soon established. She was able to enter a somnambulistic state in spite of the fact

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that labor contractions were already occurring every three minutes. She was given the suggestion that her pain would completely cease and that she would become relaxed, unafraid, and cooperative. The suggestions were effective almost immediately. She appeared relaxed and did not show evidence of pain, tension, or apprehension.

She was delivered of a 2,664.9-gm. (5-lb. 14-oz.) male by low forceps without premedication or any anesthesia other than hypnosis. She made no complaint of pain throughout the delivery. The muscles of the perineum were relaxed, and no laceration was sustained. Assisted respiration was continued during the delivery. Following delivery the patient was awakened after being given the posthypnotic suggestion that she would be relaxed and comfortable. The mother has made slow but continuous progress, although paralysis of muscles and weakness persist.

Case 2.—A 36-year-old female was sensitive to procaine. Because of this she objected to the use of any local anesthetic agent. For the previous three years she had refused to allow her dentist to perform even minor procedures without administration of a general anesthetic. Injection of procaine, according to her physician, resulted in severe reactions characterized primarily by edema of the face and body, urticaria, and nausea and vomiting. Since it was impractical to administer an anesthetic each time she required dental procedures, the patient soon refused to return to her dentist. Most of her teeth eventually developed caries. Because of the complexity of the total situation, we were asked to evaluate the patient as a suitable subject for the use of hypnosis as an anesthetic. Personality evaluation indicated an individual relatively free of emotional symptoms other than extreme fear of dental procedures. After a discussion of hypnosis, she proved to be an excellent subject and was soon capable of entering a state of somnambulism. Thereafter, on five separate occasions dental procedures lasting approximately two hours each were successfully performed with the patient under hypnosis. During these procedures she was free of all pain and of apprehensiveness. Eventually her fears of dental procedures were greatly diminished, and now she is capable of undergoing at least minor procedures without hypnosis.

Case 3.—A 14-year-old girl had developed epileptic convulsions after a head injury four and one-half years prior to her admission to the hospital. The convulsions occurred at the rate of two or three per day and were usually preceded by an aura consisting of a "tingling sensation in the fingers of both hands" and accompanied by a loss of consciousness of from 30 to 60 seconds. Electroencephalographic studies revealed a focal discharge in the right temporal lobe. Anticonvulsive medication was successful only to the extent of reducing the number of daily seizures.

Since conservative treatment was not considered adequate and since there was a temporal focus, it was decided to perform a temporal lobectomy with electroencephalographic monitoring. It became necessary to consider the effects of anesthetic agents given by inhalation or intravenously upon the electroencephalographic patterns. Since it is well established that there are no alterations in the brain wave patterns in even the deepest state of hypnosis,[1] it was decided to try hypnosis plus local infiltration of the scalp with procaine for the anesthesia. The possibility of using hypnosis was discussed with the patient. She proved to be an excellent hypnotic subject and was hypnotized four times before surgery to condition her to enter the somnambulistic state required for the proposed surgery.

At operation the scalp line of incision was injected with a 2% solution of procaine. She was then hypnotized and, after she had entered a state of somnambulism, the surgical procedure was started. During most of the operation the patient was relaxed and comfortable. She did, however, complain of a mild pain while the dura was being separated from the bone. Twice during the nine-hour procedure it was necessary to inject the scalp with additional local anesthetic because of the patient's perception of pain, especially upon forceful retraction of the scalp margin. The abnormal spiking electrical focus was confirmed by electroencephalographic tracings, and the proposed excision of the focus was performed. The patient did not complain of pain during this excision except on one noteworthy occasion when, as a blood vessel in the hippocampal region was being coagulated, the patient suddenly awoke from the hypnotic trance. She was immediately rehypnotized and was able again to enter a deep state of somnambulism. (The fact that the patient woke from the hypnotic state when the hippocampus was stimulated has led to considerable interest and speculation on our part as to the neurophysiology of hypnosis, and it opens another avenue for investigation.) The final electroencephalographic tracings revealed no further abnormalities. After electroencephalograms were completed, the patient was given 100 mg. of thiopental sodium intravenously. She remained in excellent condition throughout the procedure. Upon completion of the operation, she was able to answer questions but was amnesic concerning the surgery because of a posthypnotic suggestion given prior to awakening. She had also been given a posthypnotic suggestion that she would experience a prolonged sleep, which she did for six hours without further sedation. The postoperative course was very satisfactory and free of complications.

Case 4.—A 33-year-old male had thermal burns covering 45% of the body surface. During the first phase of treatment he required numerous changes of dressing and débridements. It soon became necessary to administer a general anesthetic for these changes because of pain elicited in manipulating his extremities during the procedure. He became progressively fearful of the frequent anesthesia and was generally withdrawn, negativistic, and uncooperative. Therefore, it was decided to use hypnosis as an analgesic during these changes of dressing and débridements. The patient was a good hypnotic subject, and the hypnotic procedure was successful both as an analgesic and in improving the patient's general mental state. Hypnotic sleep was used as the anesthetic agent during the next surgery. Extensive débridement was carried out and a split-thickness skin graft was taken from the right leg. He was given the posthypnotic suggestion that he would perceive no pain in the donor area or in the area of débridement. Upon his awakening, the suggestion was in effect. Two days later the sensations of pain and touch were restored by hypnotic suggestion. The patient's recovery was rapid and without complications.

Case 5.—A 34-year-old single female with severe congenital heart disease had repeated x-ray examinations over a period of years that revealed an extension of the pulmonary artery shadows with congenital changes consistent with a diagnosis of Eisenmenger's complex. Approximately six months prior to the time of referral, the patient began having extreme difficulty in her menses. Menstrual flow lasted from 15 to 17 days. At the onset of such a period, bleeding was described as excessive and heavy, resulting in spotting during the last few days. A pelvic examination revealed the patient to be a nulligravida with a virginal introitus. Because the hymenal ring was so tight and because the patient was extremely anxious and tense, her gynecologist was unable to perform an adequate pelvic examination. The gynecologist was of the opinion that dilation of the cervix and curettage of the uterus were indicated for purposes of diagnosis. However, both the gynecologist and cardiologist felt that the patient presented a definite anesthetic risk. Although it was agreed that a caudal or a saddle block would be acceptable, it was also agreed that hypnosis might be safer if the patient were a suitable subject.

Personality evaluation revealed that the patient was very immature emotionally and highly dependent on her mother. Her social activities were limited and were always approved by the mother beforehand. She seldom dated and was extremely naïve and fearful of any kind of sexual activity, preferring not to be alone in the company of men. Because of her emotional immaturity and numerous neurotic conflicts, it was feared that the extensive use of hypnosis might arouse more overt symptoms of psychiatric illness. However, it was decided that this risk was worth taking because of her physical status. After reasonable rapport had been established with the patient and the possible use of hypnosis had been explained to her, she accepted the proposal, although she was obviously anxious about how she would respond to this method and whether she would be a good subject.

Actually she turned out to be a good subject and was hypnotized three times prior to surgery to condition her to enter a state of somnambulism. A pelvic examination was done by the gynecologist during the third session. It was suggested to the patient that she would be free of pain and completely relaxed during the examination. While the patient was in a state of hypnosis, the gynecologist reported that it was possible to do a very adequate bimanual examination. There was neither subjective nor objective evidence of pain, tension, or anxiety during this procedure.

The patient was operated on a week later. No medicaments were administered preoperatively. After she was hypnotized, cervical dilation was accomplished, and endometrial curettage was then performed. The patient slept throughout the entire operative procedure and evidenced no perception of pain. She was given a posthypnotic suggestion that there would be no cramping or undue discomfort. After her return to the recovery room, the posthypnotic suggestions were in effect, with no pain, cramping, or discomfort reported by the patient. At the end of the hour, it was then suggested that normal bodily sensations would return to her. She was awakened from the hypnotic sleep and was amnesic for the entire procedure. Her pulse, blood pressure, and respiration showed no significant deviations prior to, during, or after the surgery. Her recovery was uneventful and free of complications.

Comment

The five cases presented represent instances in which hypnosis was considered to have special advantages over conventional anesthetic methods. As a result of our experience with these cases, some special indications for hypnoanesthesia can be formulated. First, it is indicated in cases in which chemical analgesics and depressants are contraindicated or dangerous because of respiratory or cardiac disease. This type of indication is illustrated by cases 1 and 5. Second, it is indicated in cases in which the preferred anesthetic agent cannot be used because the patient has demonstrated sensitivity to it. This is represented by case 2. Third, hypnoanesthesia should be used in cases in which the repeated use of anesthetics tends to have a debilitating effect on the patient with an already disturbed physiology. This is frequently a problem with severely burned patients who require frequent painful changes of dressings, débridement, and skin grafts. This type is illustrated by case 4 and has been more extensively elaborated on in a previous paper[2] reporting cases in which hypnosis was used to augment ambulation and other exercises as well as to increase food intake in burned patients.

Fourth, it is indicated in patients whose apprehension and fear of general anesthesia are so great as to interfere with its smooth application or even to result in serious anesthetic risks. This type is illustrated by cases 1 and 4. Fifth, hypnosis should be utilized in patients whom it is desirable to free of some of the neurophysiological effects of the anesthetic. This is illustrated by case 3. In such a case, it was desired to avoid the effect of drugs on the electroencephalogram. In other types of neurosurgical operations, it might be advantageous to have the conscious cooperation of the patient during the operative procedure, in which case hypnosis would be an ideal type of anesthesia. Another advantage in neurosurgical cases is associated with the length of time of the operation. Hypnosis obviates the debilitating effects of prolonged chemical anesthesia.

There are definite disadvantages in the use of hypnosis as a method of anesthesia. There are, for example, many individuals who cannot be hypnotized. Furthermore, some persons who are hypnotized are not capable of entering the depth of hypnotic state necessary to produce sleep and lasting anesthetic effects. It may be originally time-consuming. It also requires special training and skill on the part of the hypnotist. There are also risks involved in hypnotizing patients who have psychological problems. A careful psychiatric evaluation should be performed prior to the use of hypnosis.

Summary and Conclusions

In a series of five cases, hypnosis was used as preferable to chemical anesthesia. The use of hypnoanesthesia should be reserved for cases with special indications, because there are definite psychological hazards to its indiscriminate use and in most uncomplicated cases its use is neither practical nor economically feasible.

5323 Harry Hines Blvd. (19) (Dr. Jenkins).

Drs. G. L. Boland, A. P. Gottlieb, H. I. Kantor, Elias Strauss, J. I. Woolf, and N. R. Luhn assisted in this study.

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The Filter Organs.—The spleen, lymph nodes, and probably all lymphatic tissue possess unique phagocytic, cytopoietic and antibody-forming capacities which are functional in immunity. . . . The immunological functions of the spleen are chiefly directed toward invading organisms and other antigens which occur in the blood because its macrophages are oriented to remove materials from the blood. The spleen, therefore, should be compared with other filter organs of the blood, i. e., the liver, bone marrow, adrenal and pituitary. Of these, the liver, probably because of its size, is of greatest importance phagocytically, but, although it synthesizes serum globulins, is probably unimportant in antibody formation . . . except after lymphatic tissue appears in the periportal connective tissue as frequently happens during intense immunization or infection. . . . The bone marrow forms antibody, but how much is not known. Although relatively insignificant phagocytically, it supplies most of the heterophils which act as a first line mobile defense in certain infections. The heterophil, however, even in pyogenic infections, is probably less important than the macrophage. . . . The adrenal and pituitary are erratic as phagocytic centers and are not important sites of the cytopoiesis of connective tissue cells involved in immunity. To them have been ascribed various functions in the destruction of lymphoid cells and the release of antibody, but the extent and true significance of the pituitary-adrenal-cortical hormones in immunity still needs clarification. . . . Thus, it is evident that the spleen is not unique among the filter organs in any single function concerned in immunity, but is unique in the heterogeneity of its functions. I shall consider in order its phagocytic function, its cytopoietic activity including the production of lymphoid cells and macrophages, its role in the formation of specific antibodies and certain little understood regulatory actions on nonsplenic antibody-forming sites.—W. H. Taliaferro, M.D., Functions of the Spleen in Immunity: Presidential Address, *The American Journal of Tropical Medicine and Hygiene*, May, 1956.

CLINICAL NOTES

A MODIFIED SPINE BRACE

Robert C. Cornell, M.D., Bangor, Maine

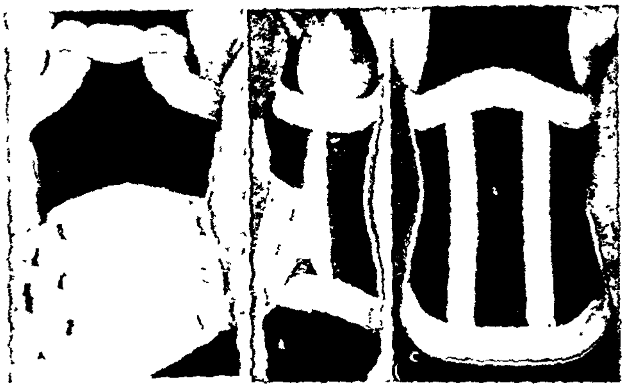
The medical literature of the past two decades is well endowed with descriptions of various types of spine braces. The majority of these are quite adequate and are as comfortable as an appliance of this type is expected to be. The brace to be described is the result of modifications of previously described braces; thus I claim little originality. In 1937, Arnold[1] described an efficient back brace. Using Arnold's brace as a pattern, I have made a number of modifications designed to increase the range of usefulness of the appliance and to increase patient comfort. In 1942, Baker[2] described a brace that he used on patients with arthritis of the spine, and Williams[3] described a brace for use in flexion management of low back conditions. Some of the ideas embodied in these two braces have been incorporated in the apparatus herein described.

Uses

As do most orthopedic appliances, this brace has its limitations, and it is not intended for the treatment of all conditions involving the spine. It is designed primarily for immobilization or stabilization of the spine from the sacrum to the seventh thoracic vertebra and is not intended for the support of the cervical and first seven thoracic vertebrae. Lumbosacral fusions can be adequately supported by shorter braces, and consequently this apparatus is not intended for that purpose. I have used this brace for the treatment of fractures of the thoracic spine distal to the seventh thoracic vertebra, thoracic kyphosis caused by juvenile epiphysitis, rheumatoid spondylitis, and incorrect posture. It has been an excellent brace for the treatment of fractures of the thoracic and upper part of the lumbar spine and has been successfully used postoperatively for fusions of the thoracic and lumbar spines. It has been used to support the spine during recovery of patients from poliomyelitis and is particularly useful in those instances in which the respiratory musculature is involved, as in bulbar poliomyelitis.

Advantages

This brace has a number of distinct advantages from the point of view of patient comfort. The apparatus is constructed from measurements taken on a flexible jig, and all components are built to conform to the contours of the patient's body. Accurate measurements can be taken in the hospital or in the doctor's office, and rarely are more than minor adjustments necessary after the brace has been completed. The brace is lightweight, easily adjusted, and may be put on in the operating room and adjusted to meet individual requirements at any given moment (see figure, A). The axillary portion of the brace does not extend high enough into the axillas to be uncomfortable and allows freedom of movement of the upper extremities (see figure, B). The lower or pelvic band is form-fitted and grips the pelvis in such a manner that the brace does not ride up or down when the patient moves. The posterior longitudinal bars (see figure, C) are placed 4 in. apart, 2 in. on either side of the spinous processes, to allow for a surgical dressing in the event that the brace is being used after a spinal fusion. Furthermore, placing the longitudinal bars in this way decreases pressure over the spine itself and adds considerably to the patient's comfort. The lack of constricting bands about the lower part of the chest makes the brace a useful appliance both in injuries in which there has been damage to the chest wall and in conditions in which there is concomitant respiratory embarrassment without injury to the patient. For instance, the brace has been used on a 6-year-old boy recovering from bulbar poliomyelitis; it supported the spine and shoulders without respiratory interference. The absence of over-the-shoulder straps makes this brace useful in instances in which there is an injury to the shoulders with concomitant injuries to the spine.



Modified spine brace. *A*, anterior view. Chest pieces can be made lower and transverse strap can be removed. *B*, lateral view. *C*, posterior view. Note space between upright bars.

Description

The brace is a singularly uncomplicated appliance. It consists of a pelvic band molded to the contours of the sacrum and ending immediately beneath the anterior superior iliac spine. Thus, the pelvic band fits well, does not slide around when the patient moves, and becomes a well-stabilized point of fixation for the lower portion of the brace. The upper circumferential band fits snugly against the upper portion of the back and varies considerably in its contours depending upon the degree of immobilization required. It extends anteriorly beneath the axillas on each side and then curves upward to end in a wide flare that conforms to the anterior chest wall in the pectoral region.

There are four longitudinal or upright bars; two are placed posteriorly 4 in. apart and the remaining two lie in the midaxillary line, one on each side. A light leather strap connects the two anterior chest pieces to prevent separation.

The circumferential bands and longitudinal bars are constructed of no. 24 S. T. Dural. The pelvic band is 1¾ in. wide and made of 18-gauge material. The upper circumferential band is 1¼ in. wide and made of 24-gauge Dural, which allows sufficient springing of the brace to facilitate its being put on and off. The upright bars are made of 24-gauge Dural that is ½ in. wide. All metal parts are padded with horse hair and felt, and then covered with elk hide. The lower portion of the brace is held in place by a wide abdominal apron with four adjustable straps. The metal portion of the brace is riveted together with rivets of stainless steel, a deterrent to rust and corrosion. The portion of the thoracic band that passes beneath the axillas is heavily padded with sponge rubber and covered with elk hide.

Summary

A simple but useful spine brace has been developed that has a wide range of usefulness and is more comfortable to the patient than previously described braces.

78 State St.

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COUNCIL ON MENTAL HEALTH

The following article is the first of a series of planned articles, which will include discussion of the medical treatment, the physiological aspects, the psychiatric aspects, and the sociologic aspects of alcoholism. After publication of the series, it is planned that the articles will be combined, along with other material, into a pamphlet on the up-to-date treatment of alcoholism as an illness, for the use of medical practitioners generally. It is the belief of the Council and the members of its Committee on Alcoholism that much of the recently developed information on the most effective methods of treating the problems of alcoholism in private practice and in hospital management has not had wide circulation and that, as a result of this, many of the patients with this illness are not now receiving the necessary attention and treatment that could and should be given them. In view of American medicine's recognition of alcoholism as a disease and not as a problem of morals, as related in the recently published statement on "Hospitalization of Patients with Alcoholism," which appears in the "Reports of Officers" in The Journal, *Oct. 20, 1956, page 750, the Council and its Committee members believe that an intensive effort is now necessary to provide these patients with the proper medical care and consideration they so urgently need.*

The next two articles in the series, as now planned, will be on the physiology of alcoholism and on the psychiatric treatment of alcoholism.

Richard J. Plunkett, M.D., *Secretary.*

MEDICAL TREATMENT OF ALCOHOLISM

Marvin A. Block, M.D., Buffalo

The medical treatment of alcoholism is rapidly becoming more important in accomplishing recovery for patients with this disease. Because of the fear and threat that so many alcoholics feel about any treatment, a medical approach seems much more acceptable. With the general feeling of physical well-being, any type of therapy becomes less of a threat and the cooperation of the patient becomes much more possible.

It is important, therefore, that the patient be given as healthy a physiological basis as is possible before any type of therapy is applied. With the newer medications at the disposal of the therapist, a medical approach can be used with much better results and fewer untoward side-effects than with the older types of medications. The medical treatment also offers an avenue for many more practitioners to treat alcoholics than heretofore, because the newer drugs allow for a greater feeling of comfort for the patient, without the lethargy that former types of therapy had produced. He is then also more receptive to other types of therapy.

The practicing physician should be equipped with knowledge of the medical treatment of this illness when he encounters such a patient. Once this treatment has produced the desired effects, other types of therapy may be employed as indicated. The following outline of treatment is intended as a general medical approach to the problem and is arranged in such order as to fit within the framework of the practicing physician's experience and knowledge of medicine, physiology, pharmacology, and psychiatry. Special cases and complications may require the aid of experts in various specialties, but, for the vast majority of such patients, this outline will serve.

Chairman, Committee on Alcoholism.

Acute Alcoholic Intoxication

The acute state of alcoholic intoxication may occur in any individual, be he an alcoholic or not. It represents a period of excessive drinking that renders the individual unable to function effectively. The intoxication may vary in the degree of intensity as well as in duration. Reactions to intoxication by alcohol have a wide range, depending upon the individual involved. There is a general characteristic behavior of acute alcoholic intoxication, but, since it varies with the reactions of the individual and depends largely upon the emotional response to withdrawal of his control, all do not react exactly alike. Without his controls, the individual will respond to various stimuli affecting his interpersonal relationships with his family, friends, employers, and fellow employees. Such relationships without control of emotions and judgment may result in severe tragedies and unpleasant consequences. When such actions are contrary to law, they may result in consequences having far-reaching effects. When they are contrary to good judgment, as in the case of automobile accidents, physical harm and even death may result.

The objective of the physician with a patient in this state of acute alcoholic intoxication is to detoxify him as quickly as possible, so that the effect of the alcohol no longer obtains. It is useless to attempt further remedial measures, such as psychotherapy, while the patient is in the acutely intoxicated stage, since there is no judgment present for him to use, nor is there sufficient understanding to make an impression when he is befuddled. This does not mean, however, that recovery during the alcoholic acute stage should not be utilized for the purpose of indoctrination. It is much more sensible, however, to wait until the patient's mind has cleared and he can understand and cooperate with the therapist.

It does not necessarily follow that psychotherapy must only be administered if the patient requests it. Such therapy can be administered without the patient being aware of it. Many such patients in emerging from their alcoholic stupor express an intense desire to be returned to the somnolent state. To accede to these wishes would only prolong the period of intoxication, whether that intoxication then be from the alcohol or from sedative drugs administered by the therapist. There are times when the patient is acutely active, when it is necessary to administer drugs as substitutes for the alcohol, but these drugs must be given judiciously and not necessarily at the patient's request. It must be remembered that alcohol acts as an anesthetic agent, with the same effect as any other anesthetic, and the same stages of anesthesia are experienced. Both during induction and when the patient emerges from the anesthetic, he goes through an active phase. With other agents such as nitrous oxide or ether, the stage is much shorter than with alcohol. Since the stage of activity with alcohol is longer than with the other anesthetic agents, it is necessary at times to use sedation to keep such activity from getting out of control. This stage of activity, when the patient is emerging from the acute intoxication of alcohol anesthesia, must often be controlled by giving sedatives.

Hospitalization

While it is not always necessary to treat the patient with acute alcoholic intoxication in a hospital, there is no doubt that this is the best setting for such treatment. It is of advantage to both the physician and the patient to have the hospital accept these patients. It is in the hospital that the laboratory procedures so often necessary can be carried out quickly and thoroughly. Intravenous therapy is readily available. Emergency measures are at hand. There is no substitute for the general hospital in caring for these patients, and anyone with experience in treating alcoholics will agree that there is very little difficulty with most of them, contrary to the general impression of some personnel. Records of hospitals that have admitted these patients will confirm the report that most of these patients offer no more difficulty than any other sick person. On the contrary, the attitude of the hospital toward the acutely ill alcoholic patient that he is sick and welcome for treatment makes these patients more cooperative than many other hospital patients. There are exceptions to this rule, of course. Patients in delirium or unusually active patients may cause some difficulties. However, with the newer methods of treatment, these phases can be passed through so rapidly that they represent no great problem to the hospital or to the physician. Even with these patients, no more help is required than with the patient recovering from an anesthetic after surgery.

There are other advantages in having the alcoholic patient in a hospital during the acute phase. All too frequently, the family of the alcoholic is in an unfavorable emotional state during the patient's intoxication. They do not know how to cope with the situation or how to react to the alcoholic's strange behavior. Some, with the best of intentions, continue to give alcohol to the alcoholic. Others, in an attempt to stop his drinking, get into difficulties with the patient suffering emotional reactions resulting from abstinence. In other instances the living conditions and environment of the alcoholic may be the specific cause for his going on his binge, and in this environment he continues to be irritated and continues his drinking. Removing him from such irritating surroundings is at least one way of helping him refrain from drinking. His presence in the hospital enables the physician to carry on with the laboratory procedures, to change medications without difficulty, to try many approaches, and in other ways to control the situation more accurately. From the point of view of the hospital, especially the teaching hospital, it gives the house staff and the nurses an opportunity to deal with these patients and to learn the various ways in which they may react. It prepares the members of the resident staff for the care of this type of patient after they leave their hospital training. None of this must imply that hospitalization is an absolute necessity for most of these patients. With the proper environment in the home, with the proper people to care for the patient, and with the necessary medication, the same type of therapy can be carried on elsewhere. Some nursing homes are well equipped for this, but for the most part they are not the ideal place to care for the acutely ill alcoholic patient.

Evaluation of the Patient's Condition

As with any other sick person, the first step in therapy is a complete physical examination and evaluation of the patient's condition. The smell of alcohol on the breath does not necessarily mean that the apparently intoxicated individual is, in reality, in a state of acute alcoholic intoxication. Other types of poison, head injuries, or other concomitant constitutional diseases may render the patient unconscious, and this type of illness must be ruled out before the patient can be said to have acute alcoholic intoxication. The smell of alcohol on the breath is not necessarily conclusive. It is here that laboratory procedures and x-rays can be of great value. Hemiplegia, diabetes, insulin shock, concussion, and many other such illnesses might give the appearance of acute alcoholic intoxication if the patient with such a condition has been drinking. In reality there may be but little alcohol present, even though the breath carries the smell, and the unconsciousness may be due to another serious physical condition. Complete physical and laboratory procedures will determine the presence or absence of such concomitant conditions. Blood concentration tests for alcohol can be very valuable, where there is grave doubt, but will only determine the depth of the alcoholic intoxication. They will not necessarily rule out any additional physical factor.

In most cases of prolonged drinking, dehydration exists. This can be corrected by reestablishing fluid balance. The addition of saline solution and dextrose or fructose will help meet this emergency. Where deficiencies of diet have existed over periods of time, this condition also must be corrected. Nutritional elements and fluids taken orally preclude the necessity for further measures in this respect. However, when there is considerable vomiting, the dehydration is usually acute and there is a lack of nutritional as well as mineral elements. Such defections can be corrected by intravenous therapy, which is easily administered. A saline solution containing 5% of dextrose may be administered in 1,000-to-2,000-cc. doses in the course of 12 to 24 hours. This can be repeated every day for three days, if necessary. The addition of an ampul of vitamin B complex and ascorbic acid insures an adequate supply of these supplements and will provide the necessary balance of mineral and vitamin content.

Among other agents used in cases of acute intoxication, many therapists believe that insulin accelerates the metabolism of alcohol in the body. To accomplish this, 20 to 45 units of regular insulin may be added to the saline solution for intravenous administration. Before administration, however, it is wise to obtain a determination of a blood sugar level to make sure that the insulin is not given during a hypoglycemic state. Medicaments employed in acute alcohol intoxication are best classified by the response of the presenting symptoms to their administration.

Drugs That Stimulate the Central Nervous System and Counteract Depression

When the patient is extremely drowsy and somnolent or severely depressed as a result of excessive ingestion of alcohol, such effects can be counteracted by the administration of caffeine and sodium benzoate, dextro amphetamine (Dexedrine), or amphetamine (Benzedrine). Another drug that has the same effect and that will counteract such depression and stimulate the central nervous system is methylphenidate (Ritalin) hydrochloride. This medicament, given in dosage of 10 mg., has been found advantageous in counteracting severe depression and somnolence. Still another drug used for the same purpose is pipradrol (Meratran) hydrochloride [alpha-(2-piperidyl) benzhydrol hydrochloride]. The dosage of this drug is 2 to 25 mg. daily, depending upon the severity of the narcolepsy or depression.[1] In severe hypotension, ephedrine may be administered subcutaneously, intramuscularly, or intravenously. For patients in the very severely depressed stage, some therapists have advocated the use of pentylenetetrazol (Metrazol), 1 cc. given directly into the vein. This should be used with caution, as large doses may cause convulsions. These analeptic agents are of value only when the patient is so depressed that he cannot be aroused or if the pulse is markedly reduced in rate or quality. In most cases where there is mild stupor present, if the pulse and respiration are within normal limits, the patient will usually rouse from his stupor after the alcohol is metabolized, without the necessity for using additional drugs.

Drugs That Depress the Central Nervous System

In treating presenting symptoms such as excitability, restlessness, nausea, vomiting, and hyperactivity, measures are sometimes necessary that will control the patient and enable treatment to continue. Although to some extent in the past the use of adrenal cortex extract and the steroids has simplified the control of the acutely ill and hyperactive alcoholic, the recent advent of the tranquilizing drugs has been of tremendous value in treatment of this stage of the illness.

Tranquilizing Drugs.—The use of these tranquilizing drugs has all but revolutionized the treatment of the acute alcoholic stage. Such drugs as reserpine, chlorpromazine, meprobamate, and promazine hydrochloride have proved of immense value in treating the acutely intoxicated patient. The patient not only is given a sense of comfort that enables him to sleep but is also relieved of his nausea and is able to eat much earlier than heretofore. Chlorpromazine is comparatively rapid in its action and can be given intravenously, intramuscularly, or orally in doses ranging from 25 to 100 mg. every four hours.[2] Dosage will depend upon the patient's reaction to the drug. Larger doses are required with some patients than with others. The potentiating characteristics of chlorpromazine must be borne in mind, since the drug increases the sedative effect of the alcohol itself as well as any other sedative drugs that may be given. In most cases, however, no further sedation is required other than administration of chlorpromazine.

Reserpine, which acts more slowly than chlorpromazine, is usually given in doses of 0.25 mg. to as high as 1 mg. every four hours.[3] Although its action is slower than that of chlorpromazine, the effect of the drug apparently lasts longer. It is well to watch the hypotensive action of this drug when it is administered, although, in patients with normal blood pressure levels, it rarely has such an effect. Chlorpromazine, on the other hand, particularly when injected intramuscularly, will often give a rather severe hypotensive effect within the first 30 minutes. This possible effect must be watched closely and the patient placed in a supine position to overcome such effect. Reserpine is the refined alkaloid of Rauwolfia serpentina, but the crude drug is also very effective in the treatment of alcoholics. It acts more slowly than reserpine, but its action may last longer. Its tranquilizing effect takes longer to produce, but the patient can be kept on a regimen of smaller doses over longer periods of time.

Meprobamate (2 methyl-2-n-propyl-1, 3 propanediol dicarbamate), commercially known as Miltown or Equanil, has also been used effectively as a tranquilizer for alcoholics.[4] It also has a decidedly tranquilizing effect upon the patient, reducing the tension and allaying some of the anxieties so common in the alcoholic. It is related to mephenesin (Tolserol), formerly used by many for the treatment of alcoholism. This will be discussed later. Doses of meprobamate vary from 500 mg. given once or twice daily to the same amount given four times a day. For maintenance therapy, dosages are usually smaller. Once the condition is stabilized, it can be maintained indefinitely on therapy with a smaller amount of this drug.

An additional tranquilizing drug, promazine hydrochloride, commercially known as Sparine,[5] is also very valuable in the treatment of alcoholism. It is given in doses varying from 25 to 200 mg. three or four times a day, depending upon the reaction of the patient to this drug. It can be given intravenously, intramuscularly, or orally and has been found to be valuable in the more acutely disturbed patient, bringing about quick sedation and tranquil sleep. The patients awaken refreshed and with a good appetite.

All of the tranquilizing drugs have some beneficial effect. They produce relaxation without sleep. Their value lies in reducing tension and in allowing the patient to remain aware of his surroundings and available for psychotherapy. There have been some reports made of habituation to these drugs. However, such danger can be minimized by changing the drug at frequent intervals. There are some patients, however, who apparently become habituated to anything prescribed. Even placebos seem to offer such opportunities for these patients.

One must always look for the side-effects of these tranquilizing drugs. Chlorpromazine has been known to cause severe jaundice, and, in many cases, severe dermatitis of the allergic type. This can be counteracted by the administration of an adequate antihistaminic such as diphenhydramine (Benadryl) hydrochloride, 50 mg. three times a day. The two drugs can be given concomitantly to avoid this possibility. The latter antihistaminic is in itself somewhat hypnotic and sedative in action. The combination, therefore, with the chlorpromazine produces adequate rest as well as tranquilization. The most common side-effect of the administration of Rauwolfia serpentina or reserpine is a congestion of the nasal passages and mucous membranes. This also can be counteracted by the administration of an antihistaminic. So far there have been no great untoward reactions reported on the use of meprobamate or promazine hydrochloride. With promazine hydrochloride, one case of agranulocytosis has been reported but, on the basis of investigation, might be considered questionable.[6] Although for the most part barbiturates are not recommended for the treatment of the alcoholic, mephobarbital (Mebaral) has been recommended by some as an efficient sedative.

Many physicians treating alcoholics use these tranquilizing drugs to the exclusion of all other sedation and have obtained good results with this type of therapy. Even with patients in delirium tremens and extreme hyperactivity, these drugs have been used very effectively, although larger doses may be necessary.

Adrenal Cortex Extract.—For a long time, the use of the aqueous solution of adrenal cortex extract was popular.[7] This was administered on the theory that the glucose metabolism of the body was altered in the alcoholic and that depleted glycogen stores could be restored to normal by administration of adrenal cortex extract. It was believed by most that the adrenal cortex exhaustion in alcoholics results from continued emotional disturbances and produces upsets in the glucose metabolism. The adrenal cortex extract solution is still used intravenously by many and has been found of great help. The dosage varies from 10 to 30 cc. in 1,000 cc. of saline solution injected over a period of several hours. Where the adrenals seem to be exhausted to a greater extent and the reaction is more severe, from 10 to 20 cc. of the aqueous solution may be administered directly into the vein. It has been found to produce a very quieting effect on the patient, to reduce his anxiety, and to induce a tranquil sleep. Where the patient is extremely tremulous, from 10 to 50 cc. of mephenesin aqueous solution may be added. Although the relief from the tremors in these cases is temporary, it does help the agitated patient.

Paraldehyde.—Another drug that has enjoyed great popularity for many years among many practitioners is paraldehyde. This has long been a favorite for the treatment of the acute phase of alcoholism. However, it is little more than an effective hypnotic and renders the patient sleepy and drowsy even after awakening. Dosages vary from 5 to 25 cc. orally or 10 to 15 cc. intramuscularly, depending upon the size of the patient. When given intramuscularly, great care must be exercised in seeing that the drug is administered deeply into the muscle, since deposits of this drug more superficially will result in necrosis of the tissue. Paraldehyde has definite drawbacks, in that it is habituating to a great extent, and many alcoholics who have been through the acute phase on numerous occasions will request the drug when entering the hospital. The odor prevalent in the elimination by the lungs renders it unpopular on many occasions. When there is a wish to combine this drug with some of the tranquilizing drugs such as chlorpromazine, it must always be remembered that the chlorpromazine has a potentiating effect on the sedative, necessitating but a fraction of the ordinary dose of paraldehyde.

chotherapy is necessary, the problem that confronts the therapist is to keep the patient from resorting to alcohol during such period of therapy. Chlorpromazine, reserpine, Rauwolfia serpentina, meprobamate, and promazine hydrochloride all can be used for this purpose. The characteristics of these drugs have been described previously, and they may be used during this period of rehabilitation as indicated. Dosages vary and of course are much smaller than when used during the acute phase of the illness. Patients will react differently to these various drugs, and the medicaments can be used most effectively by adapting the therapy to that which suits the individual patient best. It is sometimes of great advantage to use combinations of these drugs, depending upon the effect on the patient. However, there is a percentage of patients who find it difficult to refrain from alcohol even with these tranquilizing medications. With this type of patient, disulfiram is a valuable adjunct.

Disulfiram Therapy

Disulfiram [bis (diethylthiocarbamyl) disulfide], known as TETD or Antabuse, is a drug designed to keep the alcoholic from drinking. Ingestion of alcohol while under this therapy results in an episode of severe and intense illness, which is so disquieting that knowledge of such a reaction acts as an excellent deterrent. Disulfiram itself has very little effect upon the body. Some patients might complain of fatigue, a slight loss of sex potency, an occasional skin allergy, some headache, some malaise, but generally speaking it is tolerated without any difficulty. Occasionally it causes gastric distress. With the ingestion of the slightest amount of alcohol, however, a succession of symptoms occurs that causes extreme discomfort.[11] Within a few minutes of alcohol ingestion, there is a flushing of the face that extends down over the neck and chest and becomes deeper and deeper until the skin is bright red. There is a sensation of great heat in the area, followed by a pounding headache that becomes very severe. The blood pressure rises suddenly with this headache, but within a few minutes there occurs a precipitous drop in the blood pressure, giving the patient a sense of faintness and nausea, sometimes followed by violent vomiting. The patient may break into a cold sweat and often complains of extreme pain in the precordium, simulating a coronary heart attack. The discomfort is very severe and may last from one to two or even four hours, depending upon the amount of disulfiram and alcohol that has been ingested. The patient subsequently falls into a deep sleep, which may last for several hours.

When this drug was first used, it was thought necessary that it be administered in a hospital setting. After the patient recovered from the acute intoxication disulfiram was given and the patient subjected to the alcohol test. He was given 0.5 oz. of whisky and allowed to experience the sensations described. In this way he learned what would happen should he drink alcohol while under disulfiram therapy. For some time now, it has been thought unnecessary to subject the patient to this experience. The mere description of what will happen is sufficient for the average patient to understand the risks involved in drinking alcohol while taking this drug. Where doubt does exist and the patient decides to experiment, only a small amount of alcohol is sufficient to convince him of the effect of disulfiram. It is necessary, however, for the therapist to describe accurately to the patient the risks involved and what will happen, so that there will be no doubt in his mind that drinking alcohol will result in serious consequences. In addition, he is given a card to carry with him, identifying the patient and his physician, explaining that he is under disulfiram therapy and that no alcohol should be administered should he be found in an unconscious state. The description of this procedure is by far, in most cases, sufficient to convince the patient of the seriousness of this type of treatment.

In those cases where the patient does take alcohol while under disulfiram therapy, it is well to know the antidotes that can be used. Recommended measures are putting the patient in shock position and injecting ascorbic acid intravenously. If the patient is unconscious, caffeine and sodium benzoate may be administered intramuscularly. Dextrose and saline infusions are also recommended, as well as plasma, and oxygen when indicated. A good antihistaminic may be administered intramuscularly or intravenously, and diphenhydramine (Benadryl) hydrochloride has been used this way effectively. Another method of counteracting the effects of the disulfiram-alcohol reaction is the administration of chlorpromazine intramuscularly in 50-to-100-mg. doses. This usually induces a calming sleep, and the patient will awaken refreshed without the untoward effects that the reaction usually gives.

Contraindications to disulfiram therapy have been noted. They are cases of severe heart disease, including coronary heart disease, cirrhosis of the liver, epilepsy, drug addiction, psychoses, kidney disease, diabetes, pregnancy, and asthma. Some therapists have used this type of treatment with all of these types of cases without too much difficulty. However, unusual caution must be observed when doing so.

One of the risks in the use of disulfiram therapy is the possible occurrence of a psychosis. It was thought that psychoses occurring while this drug was being used were due to the toxicity of the drug itself. However, now it is believed that it is not the drug but the inability of the patient to escape into his alcoholic oblivion as an outlet for his emotional instability that precipitates the psychotic episode. It has been found that, with further psychotherapy, these patients have been able to take disulfiram again without having any psychotic reaction, even though the dose of disulfiram was exactly the same as before their psychotic episodes. It is wise, therefore, that a psychiatric evaluation be done on the patient before giving disulfiram therapy if severe mental involvement is suspected.

The reaction to alcohol of the patient taking disulfiram is due to the increase of the acetaldehyde content in the blood. In the metabolic breakdown of alcohol into acetaldehyde, acetic acid, carbon dioxide, and water, this process is arrested at the acetaldehyde stage by its contact with disulfiram and the subsequent chemical and enzyme reactions. Since acetaldehyde is a very severely toxic agent, the results that follow ingestion of alcohol are due to the increased acetaldehyde concentration in the blood. The same symptoms can be produced by injecting acetaldehyde intravenously.

Disulfiram has other uses that have proved of value in the treatment of the alcoholic patient. Its original purpose guarantees a period of abstinence long enough for practicing psychotherapy. It can, however, also be used to determine the degree of sincerity that the patient manifests in his willingness to cooperate. After discussing the effects of alcohol ingestion while under disulfiram therapy and the length of time the influence of disulfiram exists in the body, which may be from 24 to 72 hours—in rare instances as long as a week—a disulfiram tablet may be offered the patient. If he swallows it without hesitation, it would be indicative of his motivation and incentive toward abstinence. However, if he demurs, refuses, delays, or in any other way resists taking the pill, it is assurance that he still has many reservations about following through with the rest of his program. The greatest value to the patient on disulfiram therapy is the revelation that he can live without drinking. Very often after long periods of abstinence he can appreciate how much he has proved this fact to himself.

More recently, citrated calcium carbimide has been reported to be useful as a substitute for disulfiram. It has somewhat the same effects, but is said to be devoid of undesirable side-effects sometimes encountered with disulfiram—gastric distress, drowsiness, and others noted previously.[12]

Conditioned Response Therapy

The conditioned response treatment is based upon the theory that the individual patient can be trained to a certain emotional reaction under certain defined situations. This method of therapy has been employed in many areas and reports indicate variable success. In the hands of some therapists, patients respond well to this type of therapy. With others, the success has been questionable. The treatment is carried out by administering to the patient a dose of alcohol to which there has been added some type of emetic, emetine or ipecac. Under controlled conditions, the patient is given the dose of treated alcohol and the ingestion is followed by severe retching and vomiting for some time.[13] The administration is repeated on several occasions. The theory is that, after a number of such experiences, the patient will automatically refrain from drinking alcohol for fear of the consequences. Some therapists have substituted the injection of apomorphine simultaneously with the ingestion of alcohol. This type of therapy must be carried out under controlled circumstances in order to establish the conditioned response. The treatment is usually carried out in an institution where the patient can be watched carefully over a given period of time and the administration controlled with a maximum of environmental influence.

Complications of Chronic Alcoholism

Hallucinosis.—Hallucinosis is characterized by auditory or visual hallucinations, usually auditory. It usually occurs after the patient has been detoxified. The hallucinations are less severe than with delirium tremens. Differentiation from delirium tremens is important and can usually be determined by the orientation that is present with hallucinosis and absent with delirium tremens. Sedation with the tranquilizing drugs until the phase of hallucinosis is passed is the treatment of choice. However, corticotropin in 25-mg. doses given intramuscularly or intravenously every four hours for six doses has proved effective. The panic and fear associated with delirium tremens is usually not present with this complication.

Recently, azacyclonol (Frenquel) hydrochloride in doses of 20 mg. three or four times a day has also been used for this complication. It is specifically valuable for hallucinosis and has been found very effective.

Delirium Tremens.—Delirium tremens is fairly common and occurs after prolonged drinking. It may also occur upon withdrawal of alcohol after prolonged drinking. The characteristics of this condition are intense excitement, delirium, and coarse tremors. It may be accompanied by convulsions of the grand mal type. Present also is marked confusion with disorientation, which differentiates this condition from hallucinosis. Both auditory and visual hallucinations are present as a rule. These hallucinations are extremely vivid and often take the form of animals all over the room and the patient. Bizarre combinations of animal bodies and human heads and vice versa are present. Physical findings usually include dilated pupils, flushed skin, subnormal temperatures (unless intercurrent infection is present), and profuse sweating. Minute petechial hemorrhages of the brain may occur during this stage and often give rise to persistent tremors.

Treatment consists of the measures used for patients in the acute alcoholic state. The tranquilizing drugs have been recommended by many therapists and chlorpromazine and promazine have both been used to advantage.[14] These can be given intramuscularly or intravenously, but in my experience I have found it advantageous to combine them with other sedative drugs when the excitement in the patient is great. Administration of corticotropin in 25-mg. doses at four-hour intervals has also helped in bringing about more rapid recovery. This can be given intramuscularly or intravenously in the dextrose and saline solution.[10] After recovery from the acute delirium, the treatment is continued as in other stages of alcoholism.

Acute Gastritis and Enteritis.—This complication is usually due to chemical irritation of the mucous membrane of the gastrointestinal tract. Mental distress, anxiety, and frustration are usually associated with this irritation. Withdrawal of the alcohol will relieve the symptoms, as will gastric sedatives and bland diet. Drugs used in the usual gastrointestinal cases to reduce motility and soothe the inflamed membranes will also aid in this condition. The use of chlorpromazine and promazine hydrochloride for this condition will often allay the nausea and vomiting that accompany the irritation of the digestive tract membranes. However, it is often necessary to apply psychotherapy also in many such cases to help relieve the symptoms.

Varices of the Esophagus and Cardiac End of the Stomach.—This condition probably occurs much more commonly than is suspected. Its danger lies in the possibility of hemorrhage. Such signs as vomiting of blood, tarry stools, signs of shock, pallor, low blood cell count, or low blood pressure and other obvious evidences of acute hemorrhage must be borne in mind. At the first indication of such signs, immediate treatment should be instituted. The general regimen for acute hemorrhage anywhere may be used here, including complete sedation and quiet for the patient. Intravenous infusions of saline solution may be necessary, as well as transfusion if indicated. Where the hemorrhage continues, use of the Sengstaken or the Patton tube may be indicated. This tube is passed into the stomach and the bulb is inflated to 20 to 30 mm. Hg. The tube is left in place for 20 to 48 hours before deflation. After deflation of the tube, the patient should be observed for 12 hours to make sure that there is no recurrence of the hemorrhage. If no bleeding occurs, the tube may then be removed.

Cirrhosis of the Liver.—Cirrhosis of the liver is one of the very common complications of chronic alcoholism. While it is now recognized that cirrhosis of the liver is not due to the action of the alcohol itself, it is nevertheless one of the sequelae associated with chronic alcoholism. It has now been established that alcoholism is not the only cause of cirrhosis of the liver but that other conditions, which would be responsible for the lack of proper vitamins and minerals in the diet as well as necessary nutritional elements, are the basic cause of this disease. The liver has proved to be a very handy organ and can be subjected to a great deal of abuse before the condition becomes irreversible. Administration of the necessary vitamins and minerals and an adequate diet will usually result in the recovery of the liver to its normal function. However, in extreme cases and in cirrhosis of long duration, the destruction may be so severe that complete recovery is impossible. Proper diet, administration of vitamins and minerals, and in some cases injection of liver extract will help support the diseased organ. In some cases, surgery has been resorted to in order to establish increased circulation to the liver in an effort to relieve the portal system. However, in most cases, supportive treatment will be sufficient to correct this condition.

Less Frequent Complications.—The less often encountered complications of chronic alcoholism are given below.

Pathological Intoxication: Pathological intoxication is a severe reaction to the ingestion of alcohol. It is characterized by a precipitous and almost maniacal response to a comparatively small amount of alcohol. It is theorized that in such cases the alcohol acts as a trigger release mechanism setting off the ability to control the patient's actions. Treatment consists of heavy sedation until the acute phase passes.

Korsakoff's Syndrome: Korsakoff's syndrome is characterized by amnesia and confabulation. The treatment consists of supportive measures. Prognosis for recovery in these cases is very poor. Since it is now believed that this complication occurs as a result of inadequate diet, the necessary nutritional elements, vitamins, and minerals must be supplied in sufficient amounts.

Hemorrhagic Polioencephalitis, Superior (Wernicke's Disease): Characteristics of hemorrhagic polioencephalitis, superior (Wernicke's disease) include limited movements of the eyes due to partial paralysis of the eye muscles. Mental changes include intense excitement, convulsions, and clouding of consciousness, which may be severe enough to end in stupor and coma. There are usually pathological reflexes present with extreme tensions of the muscles. Tendon reflexes are absent. Since this complication is also considered to be the result of deficient nutrition, large doses of thiamine, adequate diet, and vitamin and mineral complements are indicated. Not uncommonly, complete restoration fails to occur. Mental confabulation resembling Korsakoff's syndrome is often a residual effect and may remain.

Marchiafava's Disease: Marchiafava's disease (primary degeneration of the corpus callosum) was once thought to be due to alcoholism. With only 100 cases reported in the literature, it was finally determined that this complication resulted not from the alcohol but from the metallic impurities found in wine as the result of processing.

Acute Lethal Alcoholism: Acute lethal alcoholism is due to ingestion of alcohol to a blood concentration sufficient to cause death. It occurs and acts the same as an overdose of anesthetic, producing death by a complete anesthesia of the vital centers of the brain.

Summary and Conclusions

In treating the chronic alcoholic, factors other than the medical and psychiatric approach must be taken into consideration. The patient's social environment, religious background, employment or industrial situation, and his relationships with family, friends, fellow employees, and others are pertinent factors. His relationships with his local health department, mental health department, Alcoholics Anonymous, and clergy are additional important contributions to treatment. In the chronic alcoholic, we are dealing not only with a sick individual but with that individual in relationship to his environment. In order to treat him adequately, all of these circumstances must be included.

In treating the chronic alcoholic, the cooperation of the patient is perhaps the single greatest factor in addition to the understanding and patience of the attending physician. Such psychotherapy as is necessary can be administered by the average physician who will take the time to understand and help the sick alcoholic. With the advent of the new tranquilizing drugs, the treatment of the acute phase has been greatly simplified. With the use of disulfiram (Antabuse), the patient can remain without alcohol sufficiently long for the interested physician to help him gain insight into his problem. Helping to give the alcoholic a healthy body so as to maintain optimum physical fitness will in itself make him feel better and more capable of meeting the problems that have induced his illness and probably caused it to continue. The physician has in the alcoholic a challenge from which he cannot retreat. To meet this challenge, he requires knowledge, understanding, and patience. If he will develop and use these qualities, the chances of his success with alcoholic patients will be enhanced and the results rewarding.

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MEDICINE AT WORK

MUSIC AS A MEDICAL TOOL

ANCIENT "TRANQUILIZER" COMES OF AGE FOR VARIETY OF PATIENTS

Fifteen miles from Boston's Beacon Hill, a dozen men and women one afternoon this month took part in a New England tradition that is over a half-century old. They gave a 45-minute concert of English hand-bell ringing before a sizable audience in Westwood Lodge.

It was no routine affair for the musicians, ranging in age from 18 to 79 years One was an alcoholic; others were suffering from deep depression, psychoneuroses, and schizophrenia. Westwood Lodge is a private sanatorium for patients with nervous and mental diseases. What made the occasion special was that some of the patients, somehow, were responding to the tuned bells when other musical instruments and treatment had failed to crack the shells enclosing their personalities. The sanatorium's medical director, Dr. Martha Brunner-Orne, beamed with delight as "Jingle Bells" and "Silent Night" chimed through the halls and into her office. She said: "It's just wonderful. This is the first time since we started bell ringing that the Christmas party has been devoted to that kind of music."

Hours of boredom for these Dutch patients with tuberculosis ended when the sanatorium director supplied harmonicas, rolled the bedridden players into a room, and started an orchestra Note the director at lower right and the overhead mirror he uses to survey the musicians

Dr. Brunner-Orne, a psychoneurologist, conceived of the bell ringing program one autumn evening in 1954 while at the piano in a duet with her violin-playing husband, Dr. Frank E. Orne, an obstetrician-gynecologist and fellow graduate of the University of Vienna medical school. Since then, officials of other sanatoriums have sought her advice on how they might organize similar projects.

The bell ringing at Westwood Lodge is but an echo of worldwide music that is being sounded again and again for its value as a medical aid. In the Juliana-Oord Tuberculosis Sanatorium at Laren, the Netherlands, 24 men and women suffering from tuberculosis of the bone lie flat on their backs as they present a a harmonica concert. Even the conductor is a patient, surveying his orchestra through a mirror over his head. The medical director, Dr. C. P. H. Teenstra, a director of Rotary International, brought in the harmonicas 15 years ago "just for fun."

At Denver, Colo., a 6-year-old boy plays "The Parade of the Wooden Soldiers," the first piano piece he mastered early in 1955 after an attack of poliomyelitis that left him paralyzed from the neck down in Children's Hospital. On the advice of a physician, Music Teacher Eva V. Welbourne placed the boy's arms in special slings attached to his armchair and pressed down each little finger on the piano keys until at last, after four months, the child's face lit up with the first notes of his own effort. Mrs. Welbourne has devised 20 methods by which students whose upper extremities are variously incapacitated can play the piano. They may use one finger, their elbows, their fists, their knuckles. For arthritics whose hands are clenched, she places a pencil between the fingers or a potato within the painful grasp—as the key striker.

What Does Music Do?

What happens when music—not in itself a cure—is used as a medical tool? For the bedridden patients with tuberculosis in Holland, the blank and boring ceiling scene vanishes in the melodious vibration of hundreds of brass reeds. Bell ringing patients in the Massachusetts sanatorium tend to develop confidence within a group, willingness to accept responsibility, and a music concentration that pushes aside thoughts of their personal problems. And in Denver, Mrs. Welbourne says of her piano students: "They become less handicapped than the man or woman who has two hands and 10 fingers, and does nothing constructive with them."

In the House of the Good Samaritan research hospital for rheumatic fever in Boston, young patients play keyboard instruments, flutes, "tunable beer glasses," and reed organs. Elsewhere, orthopedic and neurological patients are eased into shoulder movements by playing the drum, concertina, cymbals, and trombone.

Thousands of years ago, our ancestors used music as part of their magic healing rites, just as primitives in isolated areas do today. Although music had been used in mental hospitals in this country as early as 1792, it was not until World War II that it became widely accepted as a medical aid, largely because of its use in Army hospitals (there is greatest use now in the 100-odd Veterans Administration hospitals). A half-dozen schools offer four-year courses leading to a degree in "music therapy." Music is used in mental hospitals as an adjunct to shock therapy, hydrotherapy, and lobotomy—and the tonal expert must know how various types of music might affect different individuals.

For example, you can imagine the effect on a patient emerging from anesthesia of the booming of Wagner's "Ride of the Valkyries." Such heavy, dramatic music actually has caused relapses among patients in some hospitals. Well-planned programs, however, may carry rhythmical concertos for crippled children while they struggle painstakingly with finger painting and gay overtures for oldsters in lonely rest homes. The deaf place their finger tips on the instrument being played—and soon are able to coordinate vibration with the unheard or little-heard tones.

Some outstanding work in the field has been widely publicized, such as the case of Horace F., a schizophrenic pianist at Wayne County General Hospital, Michigan, who performed brilliantly on a nationwide CBS broadcast. Still untold are the stories of many other patients. *Etude* magazine observes: "In this age the musical profession treats people, not merely their diseases. And oftentimes, from this standpoint, music is 'good medicine.' "

Music Is Not a Cure

But although music is shown to be of great help in medicine, physicians generally have not been able to accept it as therapeutic in the true sense of the word. Dr. Jules H. Masserman, professor of nervous and mental diseases at Northwestern University in Chicago, says: "Music is only one of many avenues of approach to the patient when words alone, as is often the case, are inadequate. . . . We cannot invoke pompous sounding scientific formulae to the effect that 'rhythm stimulates the thalmus' or 'music reintegrates the functions of the cerebral cortex'; as a moderately well-trained neurologist who has conducted active research in the field I can assure you there is hardly a shread of valid evidence for such formulations."

Nevertheless, Dr. Masserman recognizes music's great value for patients. He has been an officer of the National Association for Music Therapy, whose executive committee also boasts such members as Dr. Karl Menninger of Topeka, Kan., and Dr. Ira M. Altshuler (a pioneer in the field) of the Wayne County General Hospital. It is part of Dr. Altshuler's thesis that music should enter on the mood of the patients. That is, for a maniac the music should be loud and fast, and then gradually become more subdued to bring about a similar response in the patient.

Dr. Emilian A. Gutheil, a New York City psychiatrist, sees great promise in music therapy, but he insists that it does not exist today. Says Dr. Gutheil: "The interest of the public in the problems of music therapy is tremendous, but so far no institution has undertaken the painstaking and difficult task of sifting those empirical findings which are scientifically acceptable. Most of the existing research groups are scattered, split in their aims, jealous of recognition, impatient of results, and too eager to obtain therapeutic tools to devote enough effort to tedious step-by-step research. We must arrive at a safe margin of predictability regarding causes and effects if we wish to 'write prescriptions' for therapeutic music selections."

The orchestra at Downey Veterans Administration Hospital rehearses for part of a recreation program for patients.

Prescriptions might very well be written in song titles if the coordinated-research challenge flung by Dr. Gutheil is taken up in earnest by the medical profession. Does the cold-compulsive like Bartok, Dixie, or Rock 'n' Roll? Would Mozart or Loesser cause more stability, better recovery, or more confusion—and with what type of patient? The questions are many, the research field is vast, the evidence is everywhere.

Dr. Wilma Donohue, gerontologist at the University of Michigan, tells of a 90-year-old woman completely out of touch with her surroundings who lived briefly in the present—smiling as a chain of associations was set up by a waltz being played on an accordion. President Eisenhower prescribed some of his own "heart medicine" from a sickbed in Denver last year when he called for selections from Brahms and Bach. Last month 1,200 guests of the women's auxiliary of the Chicago Medical Society watched as 50 patients in a VA hospital demonstrated their concept of music's role in physical and mental rehabilitation.

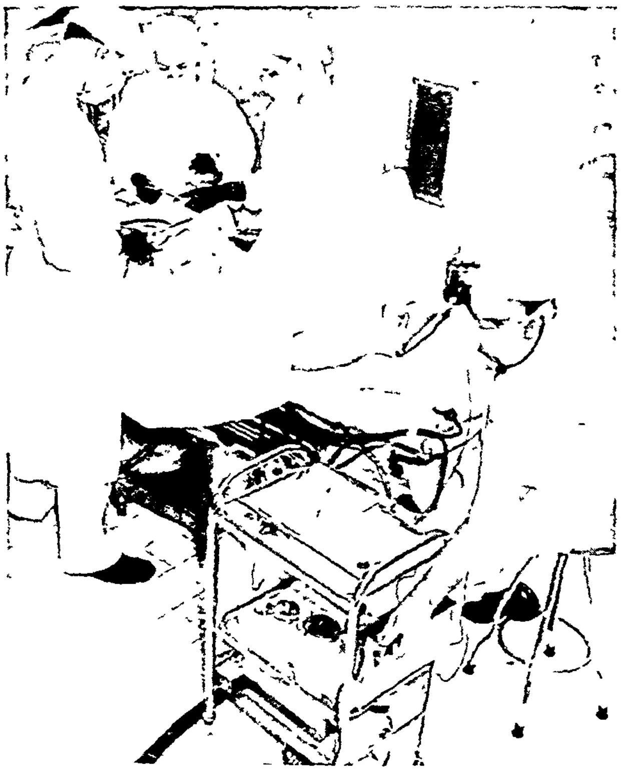
Doctors Are the Connoisseurs

There may be some significance in the fact that physicians as a group are among this nation's leading music connoisseurs. The *Saturday Review of Literature* reports: "If you took a random slice through the followers of high fidelity in any community there would be several times as many doctors in it as their number in the community as a whole would seem likely." The attendance of physicians at a Seattle Symphony Orchestra performance during the A. M. A. Clinical Session last month was greater than at any other single meeting of doctors in that city. Doctors' orchestras are making music in New York, Chicago, Detroit, San Francisco, St. Louis, and Washington, D. C. The Los Angeles Doctors' Symphony has a concert scheduled for this coming Jan. 12.

These medical men are realizing that for centuries music has been a "tranquilizer" to the healthy as well as to the sick—whether the subject produces it on an instrument or simply listens to it. Dr. Arthur Abramson, chief of physical medicine and medical rehabilitation at the Bronx Veterans Administration Hospital, claims that in some operating-room situations music may help the surgeon, the nurse, and other attendants—as well as the patient—particularly when it is played during the administration of anesthesia.

Music is piped into six operating and preoperative rooms of Billings Hospital in Chicago from a sixth-floor studio. If they wish, patients may hear their favorite selections through stethoscope-type earphones (the night before an operation, an anesthesiologist notes the patient's choice of "music for surgery"—classical, semiclassical, or pops). Officials at Henrotin Hospital, also in Chicago, still talk about the cesarean section performed on a frail little woman several years ago—with music as the chief sedative. It took three days of planning to devise the special four-hour FM broadcast musical program so that it would coincide with various phases of preoperative procedure and actual surgery.

Even at the end, music sets the tone. Not long ago in a large Midwest hospital, one physician gently closed a door on the quiet strains of a violin concerto. A young girl patient inside the room was dying, a hopeless case. Overcome with compassion, he wrote this letter to the local broadcasting station: ". . . despite extended and severe pain she had become serene and smiling during those last days filled with music in the air. Your music is a Godsend to our cases."



In a University of Chicago Clinics operating room, music with anesthesia is audible to the patient but silent to the surgeon. The anesthesiologist is also provided with a set of earphones to monitor the volume of the music for the patient.

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION
Edited Under the Direction of the Board of Trustees
Editor and Managing Publisher . . AUSTIN SMITH, M.D.
Associate Editor . . . . JOHNSON F. HAMMOND, M.D.
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Assistant to the Editor . . . . MILTON GOLIN
Editor for Medical Literature Abstracts . . GEORGE HALPERIN, M.D.
Subscription price . . Fifteen dollars per annum in advance
Cable Address . . . . "Medic, Chicago"

CLINICAL MEETING AT SEATTLE

Medical ethics, veterans' medical care, radioactive isotopes, continuance of the A. M. A. interim session, hospitalization for patients with alcoholism, and a report of the Committee on Medical Practices were among the wide variety of subjects acted on by the House of Delegates at the American Medical Association's 10th Clinical Meeting held in Seattle, November 27-30.

Medical Ethics

The subject of greatest interest was the proposed 10-section revision of the Principles of Medical Ethics submitted at the June, 1956, Annual Meeting in Chicago, where final action was deferred until the Clinical Meeting. The proposed short version of the Principles was resubmitted to the House with some changes based on suggestions received since last June by the Council on Constitution and Bylaws. The House of Delegates, however, decided to refer the matter back to the Council on Constitution and Bylaws for further study and consideration. The reference committee report adopted by the House included the following statements:

"Careful consideration was given to the Preamble and the ten sections of the proposed Principles. The Preamble and seven of the ten sections appear to be acceptable in their present form.

"Sections 6 and 7 were not acceptable as presented either to the group which appeared at the hearing or to your reference committee.

"Out of the general discussion the reference committee received the crystallized opinion that at least four areas needed more specific attention in Sections 6 and 7. These are:

"(1) Division of fees;

"(2) The dispensing of drugs and appliances;

"(3) The corporate practice of medicine;

"(4) Greater emphasis concerning the relationship between physicians and patients.

"In addition, the reference commitee felt that the wording in Section 10 could be improved if amended to read as follows:

" 'The responsibilities of the physician extend not only to the individual but also to society and deserve his interest and participation in activities which have as their objective the improvement of the health and welfare of the individual and the community.'

"In view of the above your reference committee believes that the proposed Principles of Medical Ethics should be referred back to the Council on Constitution and By-Laws for further study and consideration of the above stated principles.

"In the short space of time at our disposal and in view of the importance of the subject, your reference committee did not deem it wise to attempt to properly phrase these concepts.

"We would also recommend that if possible this study be completed at least six weeks prior to the June session and that the new version be published in THE JOURNAL in order that all interested physicians might have an opportunity to comment thereon."

Veterans' Medical Care

The House revised A. M. A. policy on veterans' medical care by endorsing in principle the following paragraph suggested by the Council on Medical Service:

"With respect to the provision of medical care and hospitalization benefits for veterans in Veterans Administration and other federal hospitals that new legislation be enacted limiting such care to veterans with peacetime or wartime service whose disabilities or diseases are service-incurred or aggravated."

This action eliminates the temporary exceptions that were made in the June, 1953, policy regarding wartime veterans who are unable to defray the expenses of necessary hospitalization for non-service-connected cases of tuberculosis or psychiatric or neurological disorders. In making the policy change, the House approved this supplementary statement:

"We recognize the laws and administrative extensions of the law that are now in operation. We feel that under the circumstances it will be to the best interests of the public in general, and veterans in particular, if medical societies, county and state as well as national, develop committees to assist in guaranteeing VA hospital admission to service-connected cases. While the present law exists, we should help assure that veterans whose illness constitutes economic disaster will not be displaced by those suffering short-term remediable ills which, at the worst, constitute financial inconvenience."

In another action concerning veterans, the House passed two resolutions condemning as unlawful the practice of those Veterans Administration hospitals that admit patients covered by workmen's compensation insurance or by private health insurance and that render bills for the cost of their care. Both resolutions requested the A. M. A. to take action to bring about a discontinuance of such practices by VA hospitals, and one of them instructed the Association's Secretary to obtain from each state testimony or records of each known case that violates VA Reg. 6047-D1.

Radioactive Isotopes

The House rescinded the June, 1951, action that limited the hospital use of radium and radioactive isotopes to board-certified radiologists by approving a new policy statement, which says:

"(1) In any hospital in which a patient is to receive radium or the products of radium or artificially produced isotopes, there should be a duly appointed

Committee on Radium and Artificially Produced Radioisotopes of the hospital professional staff. This committee should include, but not necessarily be limited to, the following qualified physicians: a radiologist, a surgeon, an internist, a gynecologist, a urologist and a pathologist. This committee should have available such competent consultation of other physicians and scientific personnel as may be required by it. Where this is not practicable, the hospital staff should consult the nearest Committee on Radium and Artificially Produced Radioisotopes.

"(2) In any hospital, the use of radium or its products and artificially produced radioactive isotopes for diagnostic or therapeutic purposes shall be restricted to qualified physicians so judged by the Committee on Radium and Artificially Produced Radioisotopes of the professional staff to be adequately trained and competent in their particular use.

"(3) It is recommended that procurement, storage, dosimetry control and inventory of all radioactive isotopes for the use of the hospital staff and radiological safety control be centralized, and, where administratively possible, centralization be located in the Department of Radiology.

"(4) It is recommended that the Board of Trustees assign to the appropriate council or committee the continuous study of the problems of radiological safety control in the use of radium and its products and artificially produced radioactive isotopes for diagnostic or therapeutic purposes."

Hospitalization for Alcoholics

To implement educational approaches to the problem of alcoholism, the House approved a statement submitted through the Board of Trustees by the Council on Mental Health and its Committee on Alcoholism. The House also recommended that the statement be brought to the attention of the Council on Medical Education and Hospitals, the Joint Commission on Accreditation of Hospitals, and the American Hospital Association. The statement includes the following section:

"The Council on Mental Health urges hospital administrators and the staffs of hospitals to look upon alcoholism as a medical problem and to admit patients who are alcoholics to their hospitals for treatment, such admission to be made after due examination, investigation and consideration of the individual patient. Chronic alcoholism should not be considered as an illness which bars admission to a hospital, but rather as qualification for admission when the patient requests such admission and is cooperative, and the attending physician's opinion and that of hospital personnel should be considered. The chronic alcoholic in an acute phase can be, and often is, a medical emergency."

Committee on Medical Practices

In approving a progress report of the Committee on Medical Practices, the House amended one of its directives to read as follows in order to remove any legal objections:

"The A. M. A. representatives on the Joint Commission on Accreditation of Hospitals be instructed to stimulate action by that body leading to the warning, provisional accreditation, or removal of accreditation of community or general hospitals which exclude or arbitrarily restrict hospital privileges for generalists as a class regardless of their individual professional competence where such policies adversely affect the quality of patient care rendered. Any action taken should be only after appeal to the Commission by the county medical society concerned."

The House also approved a recommendation by the Committee on Medical Practices that a study group be formed to consider the best background preparations for general practice, and it urged that such action be implemented as soon as practicable.

Miscellaneous Actions

Among many other actions on a wide variety of subjects, the House of Delegates also:

Pledged full support of President Eisenhower's people-to-people program as a means of promoting understanding, peace and progress;

Directed the Board of Trustees to continue its investigation of the practicability of developing a statement of A. M. A. policies and to arrange for the periodic publication of revised versions of such a policy statement;

Noted with pride the good work being done by the 74,348 members of the Woman's Auxiliary, as reported to the House by Mrs. Robert Flanders, President;

Directed the Councils on Pharmacy and Chemistry and on Foods and Nutrition to conduct a joint study of all presently available information concerning the fluoridation of public water supplies and to present a documented report of findings and recommendation at the December, 1957, meeting;

Urged all physicians to participate actively in the formulation of medical policy for prepaid medical care plans that are under physician direction or sponsorship;

Changed the bylaws to extend service membership to reserve officers on extended active duty with the defense forces and the U. S. Public Health Service;

Changed the bylaws relating to transfer of membership so that an active or associate member of the Association who moves his practice to another jurisdiction may continue his A. M. A. membership by applying for membership in the constituent association in his new jurisdiction, subject to a two-year limit on approval of his application;

Changed the bylaws so that the election of officers may take place at any time on the fourth day of the annual session, instead of being restricted to the afternoon of that day;

Passed a resolution calling for the American Medical Association to join with the American Hospital Association and the American Institute of Architects in their proposed study of hospital design and construction;

Approved the principle of a voluntary reduction in the self-assigned quota of interns as printed in the 1956 handbook of the National Intern Matching Program; and

Instructed the Board of Trustees to accentuate cooperation between the American Medical Association and the American Bar Association to the end that a bill of the Jenkins-Keogh type be enacted at the next session of Congress.

Medical School Support

The American Medical Association and four of its constituent societies—California, Arizona, Utah, and New Jersey—contributed nearly $300,000 to the nation's medical schools. At the opening session of the House of Delegates the American Medical Association announced that it was making another gift of $125,000 to the American Medical Education Foundation, bringing to $343,000 the amount that the A. M. A. has contributed to the foundation this year. In addition to the A. M. A. contribution, four state medical societies presented checks to the foundation, which will bring the contributions from physicians and medical societies to more than 1 million dollars for 1956. The states and their amounts follow: California, $132,981; New Jersey, $25,000; Utah, $11,870; and Arizona, $3,695. The practicing physicians of the nation have to date contributed nearly 6 million dollars to the foundation since it was founded in 1951. These contributions, going to the 82 medical schools in this country, can be used as the schools see fit.

Registration exceeded all expectations. The total registration was 6,282. This included 2,813 physicians. Last year's Clinical Meeting in Boston drew a total of 8,637, including 3,779 physicians. At Miami in 1954, the total was 7,707, including 3,253 physicians. A nine-page mimeographed summary of what the House did was mailed by the Secretary, Dr. George F. Lull, to all delegates and state society officers direct from Seattle, and the proceedings will be published in THE JOURNAL.

While there were many visitors who had reason to regret the fog that interfered with flying schedules, none had reason to complain about the renowned hospitality of the northwest area of the United States. This was a memorable meeting, and it ended with a note of deep appreciation of the Seattle doctors and their neighboring colleagues for the success of the meeting. No doubt many of the visitors already are planning their next trip to enjoy again the beauty of this area and what its people have to offer.

THE SCIENTIFIC ASSEMBLY AND THE SEATTLE MEETING

An unusual degree of enthusiasm marked all activities of the Scientific Assembly at the Seattle Meeting from the time Governor Arthur B. Langlie of Olympia, Wash., opened proceedings Tuesday morning until the lights were turned out Friday noon. The entire scientific meeting was held in the Civic Auditorium, making it possible for the visiting physician to go from panel discussions to lectures or to television, motion pictures, and demonstrations in the Scientific Exhibit with a minimum of delay. Various portions of the program progressed simultaneously and continuously, with only a slight lessening of the tempo during the noon hour.

The 20 panel discussions were popular, with crowded sessions most of the time. The subjects were practical, such as prenatal care, postpartum problems, pelvic pain, bleeding in pregnancy, problems of the aging, hypertension, management of low back problems, diabetes, and tranquilizing drugs. The moderators and participants of all panels were well versed in their particular subjects.

One hall was devoted entirely to lectures, which included 46 subjects covering the whole range of medicine. Many of the lecturers were from the Seattle-Portland area, making it possible for physicians from other parts of the country to obtain a comprehensive idea of the practice of medicine in the Pacific Northwest. The program included, however, outstanding men from the Middle West and the Eastern Seaboard, making this activity alone worth the trip to Seattle.

Color television was conducted with the cooperation of Smith, Kline & French Laboratories. The program, which originated at Doctors Hospital, was presented to capacity audiences at Civic Auditorium, the two-way conversations between meeting hall and operating room being especially valuable contributions. Wet clinics were conducted each morning and dry clinics each afternoon.

This motion-picture program, from the point of view of sustained interest, was one of the most successful ever conducted at a meeting of the American Medical Association. Each afternoon films were shown in Civic Auditorium, with a total of 24 titles. On Tuesday evening two films were shown at the Olympic Hotel, the first of which, titled "The Medical Witness," was presented with the cooperation of the Wm. S. Merrell Company. This was a special attraction for the legal profession as well as the medical profession and was introduced by Mr. David F. Maxwell, president of the American Bar Association. The attendance was so great that a second showing was required. Meanwhile, in an adjacent room, the film "Monganga" was presented with the cooperation of Smith, Kline & French Laboratories. This picture also attracted a capacity audience.

The Scientific Exhibit featured demonstrations continuously in 98 exhibit booths. Outstanding interest was evinced in a special exhibit on the history of medicine in the Pacific Northwest under the direction of Dr. Willard F. Goff, Seattle. The special exhibit on fractures under the guidance of Dr. Ralph G. Carothers, Cincinnati, and manikin demonstrations on problems of delivery, arranged by Dr. Charles Franklin, were always popular. Special lectures on "The Practice of Public Health and Medicine in Alaska," by Dr. Charles R. Hayman, Juneau, were especially attractive. The other 94 exhibits all merit special citation that is impossible to give. The authors were continuously present, making it possible for the visiting physician to discuss his problems and to partake in a real course of graduate medical education.

The smoothness with which all scientific activities were carried out was evidence of the meticulous care rendered by the local committee in making arrangements. Dr. Hale Haven, chairman of the subcommittee on scientific program, established an office in the Civic Auditorium, where he was continuously on duty to ascertain that all participants were present at the proper time. Dr. F. A. Tucker, chairman of the subcommittee on television, was in two places at the same time—the hospital and Civic Auditorium. Dr. Wilbur E. Watson, chairman of the subcommittee on transportation, faced an almost impossible traffic situation, with a bus strike and an insufficient number of cabs, but finally arranged special buses between the hotels and the auditorium. Other subcommittees likewise performed outstanding service. Publicity, under the direction of Dr. Earl R. Sanderson, was the best ever at a Clinical Meeting, while the entertainment, under Dr. Sydney J. Hawley, was something that everyone present will long remember. The Woman's Auxiliary, under the general chairmanship of Mrs. J. Lester Henderson, arranged a continuous program of activities for wives of physicians, ending with the special concert of the Seattle Symphony Orchestra for both physicians and wives, presented with the cooperation of Winthrop Laboratories. Dr. M. Shelby Jared, general chairman of the committee on local arrangements, overlooked no detail in making the meeting an outstanding success.

FEDERAL MEDICAL SPENDING

As physicians begin the new year, they, like most persons who earn a living, ponder the subject of income tax. At this particular time, however, most consideration is given to how much tax is due and very little thought to what it is due for. The American Medical Association's Washington Office has determined, with figures from the Bureau of the Census, that this year the average wage earner in the United States will pay about $38.72 to finance just the federal government's health and medical operations. Even with more persons now employed, this is $4.40 more than last year. If we consider the entire family of the wage earner, it will be paying $54.61 for federal medical services. Perhaps a little philosophical pondering is in order for the average physician to see just how his estimated 1956 federal medical "bill" will be spent.

About one-third of the more than 2.5-billion-dollar total of federal medical spending goes to operate the Veterans Administration, and the VA's largest single expenditure supports 121,865 hospital beds each day. Many of these are used for treatment of non-service-connected conditions. The costs of administering and supplying medical care to veterans are slightly greater than the entire medical costs of the Department of Defense, including all three branches of the armed forces. The third agency in the nine-figure category (spending over three-quarters of a billion dollars) is the Department of Health, Education, and Welfare. This comprises the medical aspects of the Public Health Service, the Social Security Administration, the Food and Drug Administration, the Office of Vocational Rehabilitation, and even the Office of Education. In actual practice much of the money covers the Hill-Burton program, the National Institutes of Health and their grants program, and grants to the states for general public health activities and communicable-disease control.

The remaining 170 million dollars supports medical activities of the Federal Civil Defense Administration, the Atomic Energy Commission, foreign health operations, and various medical programs of the cabinet-level departments. Medical care extends from the Federal Employees Health Program to coverage of residents of the Panama Canal Zone.

Many of these activities are obviously necessary to maintain this country's unsurpassed health standards, and undoubtedly research programs will pay rich dividends in procedural and scientific discoveries. Do we, however, as taxpayers as well as practitioners of medicine with a scientific background, understand the *raison d'être* for all federal medical services? Can any of the present health programs now in existence be questioned? Is the average physician contributing each month to pay for health activities that are being duplicated or that are not defensible?

Whether too much is wasted, or not enough expended, is something too difficult for any one individual to evaluate. Fortunately for all the country's taxpayers, the American Medical Association's Council on Medical Service maintains a Committee on Federal Medical Services, the prime concern of which is to educate physicians as well as the lay public on the broad scope of nonmilitary medical programs now practiced by the federal government. As one example, recent publications of this committee have served to show how over 6 million dollars is spent in the Panama Canal Zone in providing all phases of medical care to anyone, whether a resident-employee of the federal government or a person just in the Canal Zone for business or pleasure. In this particular United States community, the type of care as well as the fees are completely regulated by the government. Another example of public-fund expenditures is the medical portion of the International Cooperation Administration (known as Point 4), where almost 30 million dollars is spent organizing national and local health services in foreign countries. This money is in addition to the almost 5 million contributed to the World Health Organization and its Latin-American division, the Pan American Sanitary Bureau.

An evaluation of federal medical spending must include not only how much but, of equal importance, the precise use of each dollar. The total cost of federal health services is a billion dollars more than it takes to run the Commerce Department, and a half-billion more than all the expenses of the Department of Agriculture. It is significant that, as physicians pay their share of the public medical bill, they, because of their professional training and experience, at the same time are attempting to evaluate whether all citizens are getting their money's worth.

MUSIC THERAPY

Although music has been used as an adjunct to therapy in one form or another for thousands of years, scientific study of the relation of music to healing started about 1900. Music is no longer used to exorcise evil spirits, but the use of background music as an adjunct to physical medicine, dentistry, the induction of general anesthesia, and operations performed under local, spinal, or regional anesthesia is well known. Important as this and other passive uses of music therapy are, an even more important aspect of this form of treatment is found in active participation by the patient. Such a program finds its greatest usefulness in the treatment of patients with mental illnesses but may also be extended to a variety of other patients. Trained music therapists are being sought on an ever-increasing scale by the more progressive large general hospitals to aid in general rehabilitation programs. (Elsewhere in this issue (page 1619), "Medicine at Work" presents a detailed report on the use of music as a medical tool.)

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1. Gilliland, E. G.: Music Therapy in Rehabilitation, Hospital Manag. **81**: 46-48 (April) 1956.

On the passive side, music, properly selected for the needs of the individual patient, releases tensions and allays fears. Thus it has been found that, when it is used in the dentist's office or in the hospital operating room, music reduces the amount of preanesthetic sedation and local or regional anesthetic required. For the chronically bedridden patient it can provide a pleasant escape from boredom. On the active side, music helps mental patients to develop desirable attitudes and behavioral patterns and promotes self-confidence through self-expression; it provides the discipline of orderly activity, promotes memory, increases the span of attention and concentration, and encourages socialization and teamwork. For the patient with any disease of the musculoskeletal system, playing an instrument can be used to develop certain weakened muscles, and marching or dancing to an accompaniment may be used to improve coordination.[1] Because sounds may disturb some patients and some kinds of music may have an unwanted effect on others, all active music therapy should be conducted in a soundproof area away from the wards and music in the wards with few exceptions should be provided through individual headphones.

Just as in our schools those who are most in need of physical development often derive little benefit from the physical training program, being excluded from the teams that have become the focal point of the programs, so too those who are most in need of encouragement in musical expression are not allowed to play in the orchestra or band and must participate chiefly as listeners. The aims of music therapy in a hospital are the very antithesis of such a situation. Those who need music therapy are given every encouragement, and care is taken to emphasize the pleasurable aspects and minimize the drudgery. This may result in early performances that are musically pathetic, or even painful, but therapeutically helpful and subject to great improvement if the therapist is endowed with patience and a true desire to help the sick or handicapped. In general hospitals where an active music therapy program is in operation, concerts given by patient bands and choruses are usually preferred to those by professional groups from the outside. This fascinating field is one that has already attracted many volunteer workers. Others could do much to increase present participation in such programs.

MEDICAL CARE FOR THE NEEDY

While it has been said over and over again, it must be repeated once more—if doctors do not participate in the planning of medical care programs, they will eventually be practicing under conditions forced on them by nonmedical administrators, who have no understanding of the practice of medicine, local problems, or existing resources. Recent amendments to the Social Security Act, to become effective next year, will inaugurate an additional and at the same time separate program of medical and "remedial" care for those persons now taken care of by established public assistance programs. Many state governments are already formulating plans to take advantage of the extra grant-in-aid money this expanded federal program will allow them. It is not too early for the medical profession to ascertain who in state and local government will be responsible for administering this particular plan and to confer with these officials in order to arrange agreement between those who will superintend the program of medical care to the indigent and those who must actually provide the services.

In 1950, the Social Security Act was amended to permit states to utilize a "pooled fund" for providing medical care to the indigent. Under this plan the state deposited a specific amount of money in its medical care fund every month for each person covered by the plan. The total amount was based on the number of assistance clients and was used to finance medical care for all these persons. This system provided for medical care graduated to suit individual medical needs. It also allowed direct payments to hospitals and physicians instead of to the patient, who might not pay his bills if some other need seemed more urgent at the time his grant was given him.

The 1956 amendments affecting the assistance program formally separate federal grants-in-aid allotted for medical care from funds allocated to the four basic public assistance programs. "Public assistance," as commonly used, denotes the four federally aided assistance programs administered by the states: Aid to the Blind, Aid to Dependent Children, Old Age Assistance, and Aid to the Permanently and Totally Disabled. In addition, there are the "medically indigent" and the "general assistance" clients (insufficient income for medical care, or living expenses, but ineligible for a federally aided program). The new changes in the law not only require a separate fund for medical care, in contrast to the old method of including it in the total assistance program, but further require a fund solely for the use of vendor or insurance payments, depending on how the medical care is provided by the states.

A state does not have to participate under these new amendments, but, if it does decide to accept the increased federal money for providing medical care to its indigent, it will have to set up a formal program defining methodology. Pooled fund arrangements now in existence will no longer be eligible for federal aid; all direct payments to vendors of medical care must either come under this new program and its applicable rules or be entirely state-financed. If, however, a state does decide to participate, it is free to plan local fee schedules, capitation-payment arrangements with physicians and hospitals, or even prepayment plans on a contractual basis with state and county medical associations.

Because many physicians are accepting a responsibility to understand medical programs before they are implemented, rather than to suggest changes after the programs' inauguration, many medical care plans for the indigent function quite smoothly for all parties concerned. The Committee on Indigent Care of the American Medical Association's Council on Medical Service is investigating all aspects of the effect the social security amendments will have on medical care and is available to assist any state or local medical society professing an interest in the potentials of this new federal legislation.

THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

The 10th A. M. A. Clinical Meeting, held in Seattle last month, was exceptionally interesting and educational. The scientific program was excellent, and the physician registration was very good. For those in attendance, the postgraduate workshop of lectures, panels, television, motion pictures, and exhibits provided plenty of new ideas and procedures, and each physician was able to return to his practice with a larger fund of medical knowledge.

Special credit for outstanding work on the meeting should go to the local committee on arrangements and its general chairman, Dr. Shelby Jared; the Washington State Medical Association and its officers and staff; the state chairmen of Idaho, Oregon, Montana, and Alaska; and all those who worked out the details and who served the visiting physicians, their wives, and guests with boundless amounts of Northwest hospitality.

I am happy, too, that the newspapers and radio and television stations again did a superb job of covering the scientific sessions, the deliberations of the House of Delegates, and the various awards made during the meeting. While the Clinical Session was performing its function of getting "what's new" to the practicing physician, the communications mediums were relaying this good story of American medicine to the general public.

In my address to the House of Delegates I tried to emphasize the importance of patient and professional freedom and the need for unity, alertness, and action within our profession. I also urged that the medical profession do everything in its power to help reverse any trend toward government encroachment in the practice of medicine. I sincerely believe every one of us must talk about these three issues every time we have an opportunity to discuss them. They are vital issues for medicine, the patient and our nation.

Recently in Havana, at the World Medical Association meeting, Dr. Rolf Schloegell of Germany called freedom of the patient and the freedom of the medical profession "interacting and interdependent" freedoms and urged all doctors to assume a duty of preserving them. In this I heartily concur.

For a free people the freedom to select a medical adviser is next to the free choice of a spiritual adviser. Both should be held inviolate, and any attempt, however small, to infringe upon them must necessarily be looked upon as a move to endanger our democratic form of government.

We cannot shun our role in preserving and strengthening these freedoms. As Dr. Schloegell has said, "both freedoms are dependent on each other. As a matter of fact, one is the prerequisite condition of the other: Where there is no freedom for the patient, there can be no freedom for the medical profession, and where the medical profession has no freedom or loses it, the patient will not be able to feel that he is free himself."

Our profession does not demand "unbridled and boundless license without measure or purpose," but it does ask for freedom of choice by patients, freedom in the conduct of medical treatment, freedom of prescription, and freedom from supervision by laymen. These are medicine's four fundamental freedoms as given by Dr. Schloegell. Without them the proper patient-physician relationship cannot be created or maintained and the medical care of the patient cannot be on a private, person-to-person level.

Besides being in the best interests of the medical profession, these freedoms are in the best interests of patients, for they assure the American people of the best possible medical care. Our positive, continuing task then is to keep these freedoms. I believe one of the best ways to do so is to practice medicine with plenty of personal warmth and understanding. Let us not rely solely on our scientific skills in treating the sick. Let us combine science with the enriching forces of sympathy and personal concern. All of us should remember that new drugs, instruments, and skills are constantly replacing the old; but tender, loving care can never be replaced.

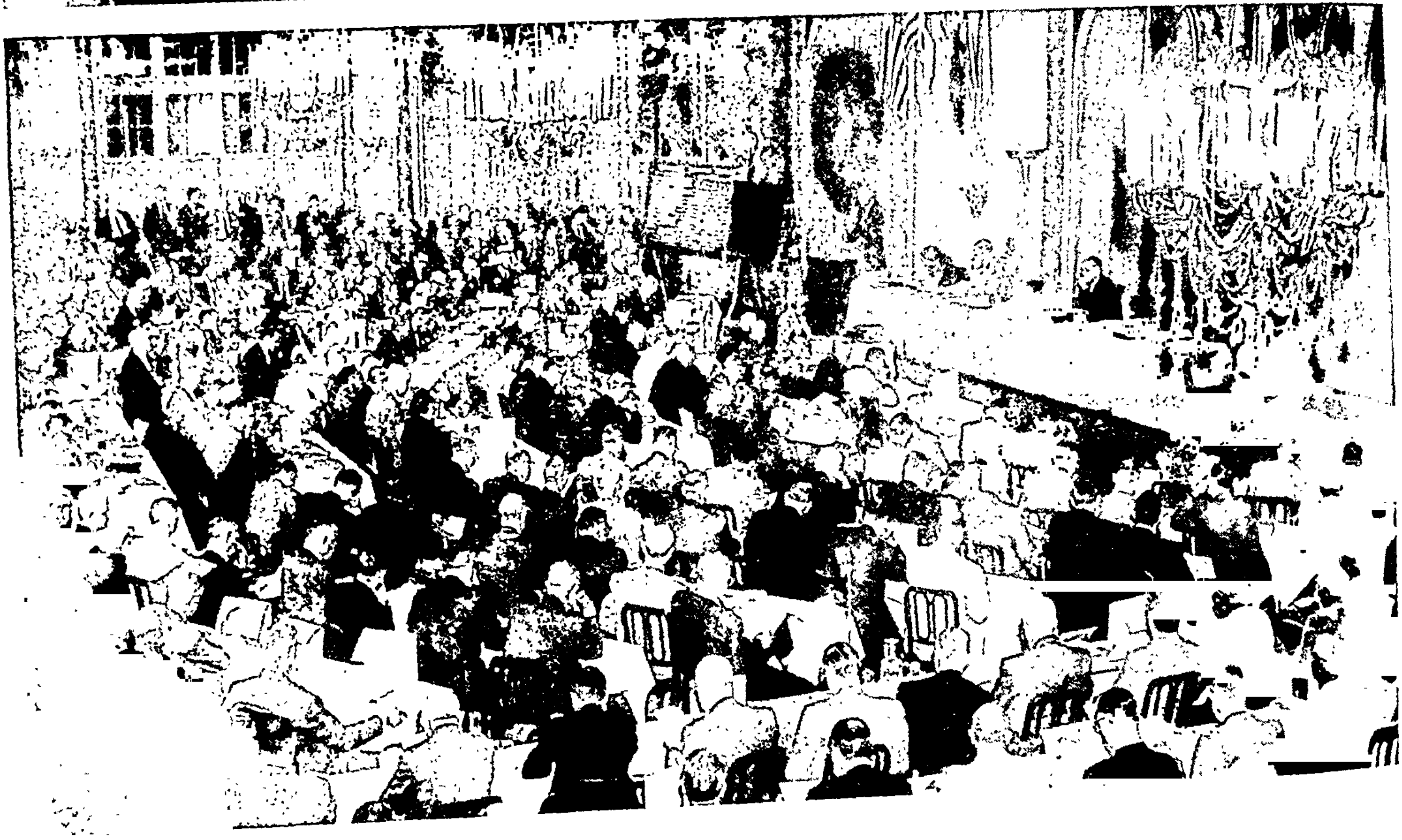
We can bolster the four freedoms of medicine by giving tender, loving care in generous quantities to all our patients. For the patient it is a medicine that works wonders in its own mysterious way. If we dispense it daily to all our patients, it will demonstrate the absolute necessity for the freedom of the patient and the freedom of medical practice, and the resulting good will among patients will be more than enough to deter, defeat, and/or shatter any force seeking to interfere with these freedoms.

DWIGHT H. MURRAY, M.D., Napa, Calif.

Seattle Meeting

Left, early morning registration as physicians entered the Civic Auditorium to attend the opening general assembly.

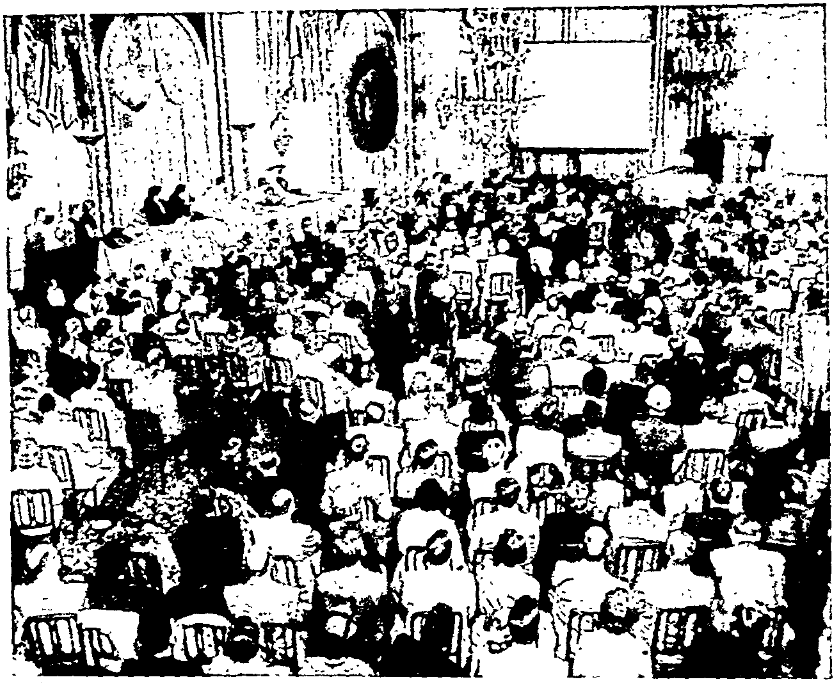
Below, the House of Delegates convened in the Spanish Ballroom of the Olympic Hotel.



Below, typical of the reference committees that study resolutions presented to the House of Delegates is the Reference Committee on Insurance and Medical Service. These committees report their studies back to the House of Delegates.

Among pre-session activities was the meeting of the A. M. A. Council on Constitution and Bylaws. Mrs. Bess Spies McDonald takes notes, as members discuss items on the agenda. Others (left to right) are Drs. Louis M. Orr; E. Vincent Askey; Floyd S. Winslow; B. E. Pickett Sr., Council Chairman; Warren W. Furey; and Walter E. Vest.

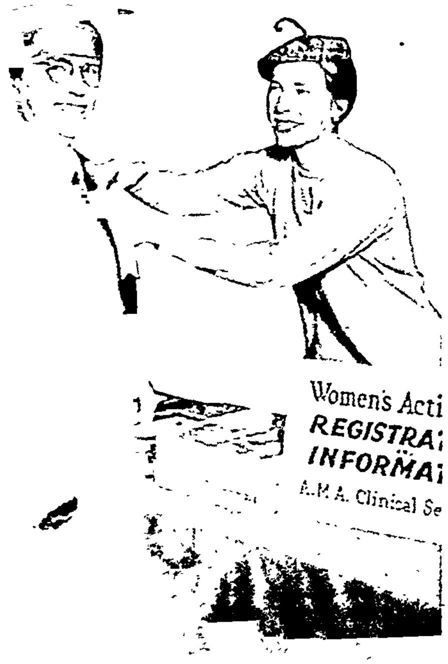
Above, a capacity-plus audience at the premiere showing of the A. M. A.'s new medicolegal film, "Medical Witness," at the Olympic Hotel.



Left, over 700 physicians and guests attended the NBC-TV showing of "Monganga," the latest in the Smith, Kline & French series on the "March of Medicine." The film, made in Africa, shows a missionary physician in practice in the Belgian Congo. It was broadcast in black-and-white and in color across the nation.

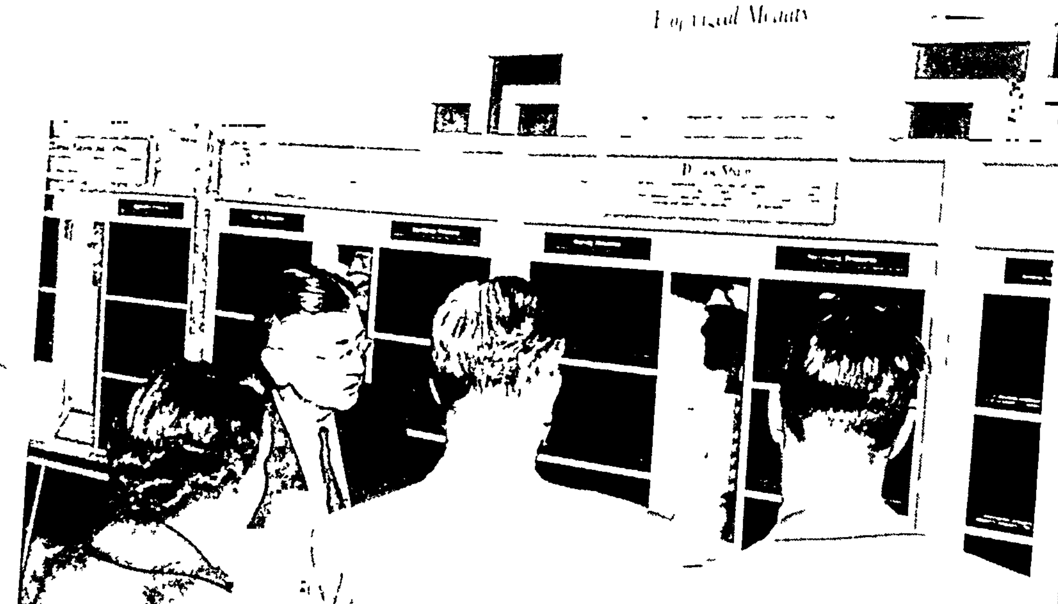
Below, at the opening general assembly of the Clinical Session, Dr. M. Shelby Jared (right), Seattle, general chairman of the local committee on arrangements, welcomed the morning speakers (left to right), Dr. James H. Berge, president, Washington State Medical Association; Arthur B. Langlie, governor of the state of Washington; Dr. Dwight H. Murray, A. M. A. President; Gordon A. Clinton, mayor of Seattle; and Dr. Elmer Hess, immediate A. M. A. past-president.

Below, Mrs. Howard K. Scatliff, Chicago, was an early registrant at the Woman's Auxiliary desk at the Hotel Olympic. Mrs. Clayton Wangeman, Seattle, representing the Woman's Auxiliary to the Washington State Medical Association, pins on an official badge.



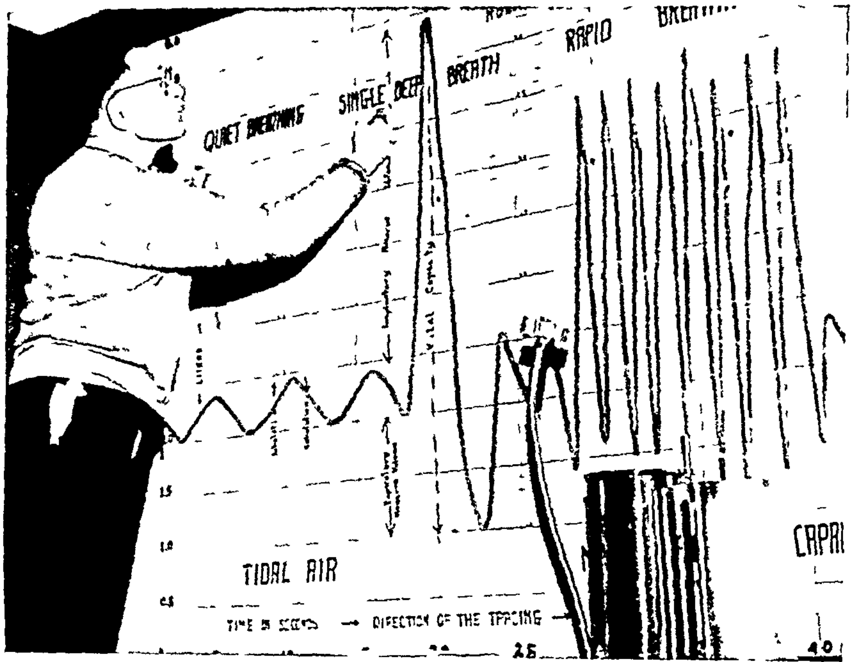
A check for $132,981 from the California Medical Association to the American Medical Education Foundation for the support of the nation's 82 medical schools was presented to Dr. Louis H. Bauer, president of the AMEF, by Dr. Donald A. Charnock (left), president of the California association, and Dr. Dwight H. Murray, A. M. A. President, Napa, Calif., before the House of Delegates.

Above, Dr. Edward M. Gans, desi nated the General Practitioner of tl Year by the House of Delegates durir the Clinical Meeting. The Harlowtoi Mont., physician is approaching th House Speakers' table to receive th gold medal award.



Above, Dr. Arthur M. Olsen, Mayo Clinic, Rochester, Minn., explains his exhibit on esophageal motility in the Civic Auditorium.

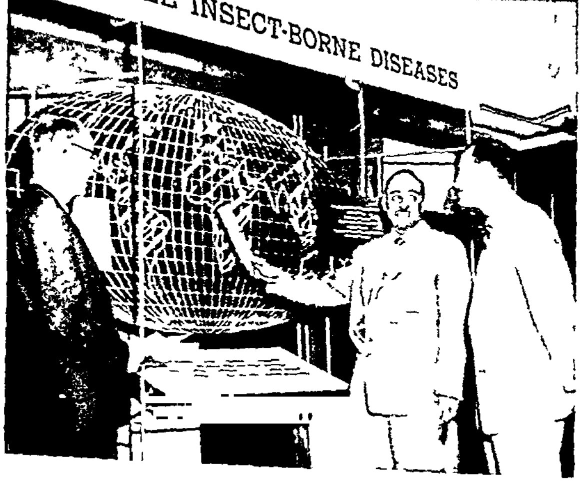
Right, in the Scientific Exhibit, Dr. Everet H. Wood of the Jackson Clinic, Madison, Wis., and the University of Wisconsin Medical School shows a series of x-rays on foreign bodies in the eye to Dr. Emma Dong, Salinas, Calif.



Left, in the Scientific Exhibit, Dr. Edward Matzger of San Francisco was among many physicians who worked over the week end to prepare their exhibits for the opening of the Seattle Clinical Session.

Below, "Fractures about the Elbow" are demonstrated as a special feature of the Scientific Exhibit by Dr. Edmund T. Rumble Jr. (right), Calicoon, N. Y., and Dr. Frederick G. Rosendahl, Minneapolis.

Below, the HEW exhibit, "Importable Insect-Borne Diseases," is explained by Dr. Glenn S. Usher (left) and J. C. Eason Jr. (center) to A. R. Ratcliff, a student at the University of Washington Medical School.



Below, Dr. Sidney Lyttle (left), Flint, Mich., and Dr. Paul Goetowski, Lincoln, Neb., demonstrate the setting of a fracture of the lower end of the radius in the Scientific Exhibit in the Civic Auditorium.

COUNCIL ON MEDICAL SERVICE

A STUDY OF MATERNAL MORTALITY COMMITTEES

This is part 6 of a series of articles by the Committee on Maternal and Child Care of the Council on Medical Service reviewing the organization and operation of maternal mortality study committees. The purpose of this specific study is to obtain information that may be utilized in the preparation of guides that, in turn, may be helpful in the development and operation of maternal mortality committees in other areas of the United States. This article is concerned with the Maternal Welfare Committee of the Wayne County Medical Society. Although this committee's study is an integral part of the total statewide study of maternal deaths in Michigan, the Detroit experience is being described separately because it indicates various differences in technique used on a local level.

Wayne County Maternal Mortality Study

History.—The first Maternal Welfare Committee of the Wayne County Medical Society was established in 1927 and, in cooperation with the Detroit Department of Health, participated in the statewide study of maternal deaths, as mentioned in the history of the Michigan State Study of Maternal Deaths. Again in 1941 a critical study of all maternal deaths in Detroit was started, but because of the war it was interrupted until 1945, when, in conjunction with the Detroit Department of Health, the study was resumed and, with slight variations in procedure, has continued to the present time. This study of maternal deaths is dedicated to the dual purpose of raising the standards of obstetric practice within the county and eliminating the preventable factors contributing to maternal deaths.

Members.—Membership in the Maternal Welfare Committee varies from 25 to 30 members, two-thirds of whom are certified specialists in obstetrics and gynecology; one is a pathologist, one an anesthesiologist, and one an internist. Members are appointed by the president of the Wayne County Medical Society upon the advice of both the outgoing and incoming chairmen. The chairman is appointed by the society president on the advice of the outgoing chairman. Many members are reappointed each year, depending upon the interest they express by attending meetings and their desire to serve. Attempts are made to assure representation on the committee of all hospitals having maternity units.

Scope of Study.—The Maternal Welfare Committee includes in its study the deaths of all women dying during pregnancy or up to six months after termination of the pregnancy. Some of the deaths may be caused by factors indirectly related to the pregnancy and involving associated disease; such deaths are included for the purpose of this study in the calculation of the maternal mortality rate. These nonobstetric deaths are defined as deaths due to disease present before or developing during pregnancy that, though not a direct effect of the pregnancy, was seriously aggravated by the physiological effects of pregnancy and caused the death; for example, deaths caused by heart disease as complicated by pregnancy would be classified nonobstetric. Maternal deaths directly related to pregnancy are classified as due to obstetric causes. An obstetric death is defined as a death due to complications of the pregnancy itself or due to intervention elected or required by the pregnancy or resulting from the chain of events initiated by the complications or the intervention. Included in this group of deaths would be, for instance, those deaths due to amniotic fluid embolism and anesthesia.

All deaths studied are also classified as to preventability and responsibility. The currently significant obstetric problems are thus determined, and the attack upon these problems can be more direct and effective. It is not the purpose of the Maternal Welfare Committee to evaluate the individual physician's competence or to censure his management of a case, but rather its purpose is to emphasize the educational aspects of the cases discussed. The study is designed to be a postgraduate course in the complications of obstetrics. All maternal deaths that occur in Detroit and Wayne County are studied by the committee, but for statistical purposes the ones that are in the nonresident group are reallocated to their county or state of residence.

Operation: Agencies and Personnel Involved.—The Wayne County Maternal Mortality Study has been in continuous operation since its resumption of activities in 1945 at the close of World War II. Since 1950, when the Michigan State Maternal Mortality Study was resumed on a statewide basis, the Wayne County study became an integral part of the total state study. It is a cooperative undertaking of the Wayne County Medical Society, the Michigan State Medical Society, the Michigan Department of Health, and the Detroit Department of Health. As a part of the statewide study, a regional consulting obstetrician (Board certified specialist in obstetrics and gynecology) is assigned to the Detroit area by the state committee. Because the Detroit and Wayne County area has a great many more maternal deaths than does any other area of the state (approximately one-half of the state total), additional obstetricians are appointed jointly by the Wayne County Maternal Welfare Committee and the Michigan Department of Health to assist in the collection of data. The Michigan Department of Health pays these consultants on a case basis as it does the other regional consulting obstetricians throughout the state.

Committee members are W. L. Crawford, M.D., Chairman, Rockford, Ill.; *R. B. Chrisman Jr.*, M.D., Coral Gables, Fla.; Philip S. Barba, M.D., Philadelphia; Harold S. Morgan, M.D., Lincoln, Neb., J. L. Reichert, M.D., Chicago; *Garland* D. Murphy, M.D., El Dorado, Ark.; Howard A. Nelson, M.D., Greenwood, Miss.; and Donald A. Dukelow, M.D., Consultant, Chicago.

The Detroit Department of Health is represented on the Maternal Welfare Committee by its chief of Maternal and Child Health, who also is the secretary of the committee. Stenographic and mimeographing services are provided by the Wayne County Medical Society. The Michigan Society of Obstetricians and Gynecologists has a maternal welfare committee that acts in a liaison capacity between the Michigan State Maternal Mortality Study and the Wayne County Maternal Mortality Study. The two medical schools in the state—the Wayne University College of Medicine in Detroit and the University of Michigan Medical School in Ann Arbor—participate in both the state and Wayne County studies through representatives from their departments of obstetrics and gynecology. The chiefs of both the departments are members of the evaluation subcommittee of the Maternal Health Committee of the Michigan State Medical Society and in that capacity review each maternal death that occurs in Michigan.

The Office of the Division of Maternal and Child Health of the Michigan Department of Health notifies the Wayne County regional consulting obstetrician of a maternal death that has occurred in his area. (All deaths in Wayne County are first reported, of course, to the Detroit Department of Health.) However, before the regional consulting obstetrician makes arrangements for visiting the attending physician and the hospital in which the maternal death occurred, he usually sends to the attending physician a questionnaire or basic information form. The attending physician returns this questionnaire to the regional consulting obstetrician. In this way the latter obtains pertinent preliminary information that facilitates his planning for the collection of data. It also gives the attending physician in the case an opportunity to make a better compilation of his records before the regional consulting obstetrician interviews him. At the interview the consulting obstetrician obtains detailed firsthand information, often personally reviewing the physician's office records of the case. He obtains the autopsy reports and other pertinent information from the hospital records.

After the regional consulting obstetrician obtains all his material and makes a summary of the case and an evaluation of the various facilities and services that the patient had received, he sends this information to the Michigan Department of Health, where all identifying data are removed. A duplicate of the anonymous material is then forwarded to the Wayne County Maternal Welfare Committee. The original is sent to the chairman of the evaluation subcommittee of the Michigan State Medical Society. After receiving his copy, the chairman of the Wayne County committee prepares a uniform protocol of the case. Prior to the meeting at which the case will be discussed, a copy of the protocol is sent to the attending physician, along with an invitation for him to attend. Copies are also sent to all members of the committee and to the obstetric departments of the hospitals in Wayne County. The chairman assigns to various members of the committee the specific task of the opening of the discussion. Prior to the meeting, these persons have studied thoroughly the particular cases to be discussed and generally have acquainted themselves with past and recent literature on the particular complications under study. All medical students, interns, and residents are invited to attend; the time of the meeting is always announced in the *Detroit Medical News*, the weekly news magazine for doctors of medicine published by the Wayne County Medical Society.

At the meeting the discussant, assigned by the chairman, presents the case and gives his analysis as to how he thinks it should be classified. Various points in question are discussed by members of the committee and by anyone else in the audience who wishes to present his views. If the attending physician is present, or if anyone else is familiar with the case personally, he is asked to contribute any additional information that he may have. If the maternal death happens to have occurred at one of the osteopathic hospitals in Detroit, it is treated in the same manner as if it had been in one of the regular medical hospitals. The osteopath in question is sent a basic information form and is visited in the same manner as is a regular physician, but he is not invited to the committee meeting.

As a precautionary measure, a case is not discussed or the protocol sent to the committee members until six months have elapsed from the time of death. Two or three cases are discussed at each meeting; these are held at a regular time each month and last about an hour and a half. An outline form for committee evaluation is appended to the case protocol; the consensus of the committee is obtained as to whether it was a maternal death, whether there were obstetric complications or other associated disease, and, with their judgment being based upon the academic ideal, whether the death was preventable.

It is the opinion of the committee that the factors contributing to maternal deaths must be examined critically and that they must be assessed conscientiously in relation to the best possible standards of medical practice. Their concept of preventability involves three assumptions: (1) that the physician possesses all the knowledge currently available relating to the factors involved in a death; (2) that he has reached a high level of technical ability; and (3) that he has had available to him all the facilities present in a well-organized, properly equipped hospital. The responsibility for death is assigned to the patient, physician, consultant, hospital, or any combination of these. In the discussion of the case the factors that are involved are determined. These are listed and involve one or more of the following categories: (1) prenatal care, (2) technique, (3) no or incompetent consultation, (4) recognition of complications, (5) management of complications, (6) inadequate facilities, and (7) any other factor. The underlying cause of death is determined, if possible, and other contributing causes are listed.

After summarizing the committee's discussion of each case, the secretary includes that information in a letter, the first and last paragraphs of which are of standard form describing the purposes and principal aims of the Maternal Welfare Committee. The letter is so worded that the attending physician who receives it will know that the committee is not criticizing him or censuring him for his management of the particular case. If the case is considered preventable, various recommendations are given, which, if followed in the future on similar cases, would perhaps not result in death of the patient. It is explained that the committee's evaluations are completely without bias and that the identity of the patient, the attending physician, and the hospital are unknown to the committee and those present at the discussion. Further, the committee extends a cordial invitation to the physician to come to any of its meetings and to take part in its discussions if he so wishes.

TABLE 1.—*Live Births, Maternal Deaths and Rates per 10,000 Live Births as Recorded by the Detroit Department of Health and the Maternal Welfare Committee of the Wayne County Medical Society, for the Years 1948-1952**

		Maternal Deaths		Rate/10,000 Live Births	
Yr.	Live Births, No.	Dept. of Health	Committee Study	Dept. of Health	Committee Study
1948	48,197	45	53	9.3	10.9
1949	50,348	37	37	7.3	7.3
1950	52,338	31	34	5.9	6.4
1951	55,300	44	42	7.9	7.5
1952	57,115	35	40	6.2	7.0
	263,298	192	206	7.3	7.8

* From Ott.[1]

Follow-Up.—In addition to the letters sent to the attending and consulting physicians in the case, a summary of the findings is also sent to the administrator of the hospital and the hospital department chief. Each year the Maternal Welfare Committee makes its report to the Wayne County Medical Society; this is printed in the *Detroit Medical News.* The report is a complete account of the number of deaths studied by the committee, with tables showing the causes of death, preventability, and the factors of responsibility. The factors are listed in the order of relative importance in each of the three categories: physician responsibility, patient responsibility, and hospital responsibility. A brief discussion is usually included on the important obstetric hazards that have been brought to the attention of the committee in their study; suggestions are made as to ways and means of lessening those hazards.

A five-year study of maternal deaths in the city of Detroit during the years 1948 through 1952 was presented to the Michigan Society of Obstetricians and Gynecologists at their meeting in February, 1955. These obstetricians and gynecologists devote one of their meetings every other year to discussion of the study made by the Maternal Welfare Committee of the Wayne County Medical Society; one meeting in each alternate year is devoted to a discussion of the statewide study.

TABLE 2.—*Causes of Maternal Deaths, Number and Percentage of Such Deaths and Autopsies Performed, 1948-1952**

	Deaths Studied		Autopsies Performed	
Cause	No.	%	No.	%
Hemorrhage	78	37.9	35	44.8
Cardiovascular	43	20.8	19	44.2
Toxemia	31	15.1	10	32.3
Infection	23	11.2	13	56.5
Anesthesia	12	5.8	5	41.7
Miscellaneous	19	9.2	9	47.4
Total	206	100.0	91	44.2
Nonrelated deaths	49	19.2	21	42.8
Total deaths studied	255			

* From Ott.[1]

Brief specific articles regarding various obstetric problems are prepared and published from time to time in the *Detroit Medical News.* The committee has initiated efforts to publicize the need for education of the laity and their part in preventing maternal deaths; it has met with the press in order to provide material for stories on the function and achievements of the committee; programs for radio and television have also been developed.

Material gained from the study by the Maternal Welfare Committee in Detroit has been the source of information used by members of the committee for preparation of papers presented before other state medical meetings. These papers are published in the various state medical society journals and, therefore, afford an opportunity for physicians in other states to become acquainted with what is being done in Michigan and Detroit. These articles have not only been published in state journals but have appeared in such national journals as THE JOURNAL of the American Medical Association and the *American Journal of Obstetrics and Gynecology.*

In order that the program of the Maternal Welfare Committee will be familiar to graduating students of medical schools, the committee conducts occasional meetings or obstetric seminars at the Wayne University College of Medicine. In addition, several hospitals have requested talks by committee members to both their total members and their intern and resident staff on current problems in obstetrics as brought into focus by the committee study.

TABLE 3.—*Distribution of Patients with Obstetric Complication, Associated Disease, and Preventable Factors in the 206 Deaths Classified as Maternal by the Maternal Welfare Committee, 1948-1952**

		Obstetric Complication		Associated Disease		Preventable Factors	
Cause	No.	No.	%	No.	%	No.	%
Hemorrhage	78	78	100	13	16.6	73	93.6
Cardiovascular	43	22	51.2	39	90.7	29	67.2
Toxemia	31	31	100	12	38.7	30	96.8
Infection	23	23	100	7	30.4	22	95.6
Anesthesia	12	12	100	4	33.3	10	83.4
Miscellaneous	19	16	84.2	10	52.6	9	47.4
Total	206	182	88.3	85	41.3	173	84.0

* From Ott.[1]

Results: Statistical Analysis.—Two hundred fifty-five deaths were studied during the five-year period from 1948 to 1952; the Maternal Welfare Committee classified 206 of these as maternal deaths, that is, deaths due to both obstetric and nonobstetric causes, and 49 as deaths caused by nonrelated factors. The Detroit Department of Health, over the same period of time, classified 192 of them as maternal deaths. Table 1 shows the relationship of live births, maternal deaths, and the rate of maternal deaths per 10,000 live births as recorded by both the Detroit Department of Health and the Maternal Welfare Committee of the Wayne County Medical Society. The Detroit Department of Health statistics for the next three-year period (1953-1955) was 4.0 per 10,000 live births (0.4 per 1,000 live births); this is indicative of the progress being made in Detroit. The 206 deaths classified as maternal by the Maternal Welfare Committee were further classified according to cause of death into six categories as indicated in table 2. The percentage rates of these chief causes are given, plus the number and percentage of autopsies performed.

Table 3 further breaks down the six categories of the causes of maternal death into those due to obstetric complications and those due to associated disease; it also gives the number of cases in which preventable factors were found to exist. Table 4 is a detailed analysis of the 206 maternal deaths relative to the number and percentage with preventable factors and major responsibility assignment. It is noted that the major responsibility in 71.9% of these deaths with preventable factors was assigned to the physician; only 9.7% were assigned to the patient and 2.4% to the hospital. Of the 206 deaths that the committee considered maternal, 11.6% were classified as not preventable; preventability factors and responsibility could not be determined by the committee in the remaining 4.4% of the maternal deaths. In regard to the product of the pregnancy in the 206 maternal deaths, analysis indicates 90 live births, 55 fetuses born dead, and 28 fetuses not delivered; 33 cases were due to either ectopic pregnancy or a resultant abortion.

The Maternal Welfare Committee made further detailed analyses of these maternal deaths. The six categories of the causes of maternal deaths were correlated to (1) the method of delivery; (2) various terminations of pregnancy other than regular delivery; and (3) patient factors of preventability, such as the patient's delay in seeking initial care or delay after symptoms and her failure to appear for appointments or to follow the advice of the physician. The largest factor in patient preventability was that of delayed initial care; this accounted for 44.2% of the deaths classified as preventable and the responsibility of the patient. Detailed analyses of the factors causing the maternal deaths that were assigned as the responsibility of the physician indicate that inadequate or improper treatment accounted for 32%; 22.7% were due to complications that the physician failed to recognize; and 19.7% showed poor or no evaluation of hazards. Improper timing of operation, the use of an improper drug or procedure, and failure to seek consultation accounted for the remaining 25.6%. In the deaths considered in some degree to be the responsibility of the hospital, inadequate professional standards was the factor in 26, or 40.6%, of the cases; inadequate facilities in 24, or 37.5%; and inadequate personnel in 14, or 21.9%.

Table 4.—*Maternal Deaths, Preventability and Responsibility, 1948-1952**

		Preventable Factors						Not Preventable		Not Determined	
		Patient		Physician		Hospital					
Cause	No.	No.	%	No.	%	No.	%	No.	%	No.	%
Hemorrhage	78	7	9.0	65	83.3	1	1.3	5	6.4	..	...
Cardiovascular	43	3	7.0	26	60.5	..	...	13	30.2	1	2.3
Toxemia	31	3	9.7	27	87.1	..	...	..	...	1	3.2
Infection	23	5	21.7	16	69.6	1	4.4	..	...	1	4.4
Anesthesia	12	..	...	9	75.0	1	8.3	..	...	2	16.7
Miscellaneous	19	2	10.5	5	26.3	2	10.5	6	31.7	4	21.0
Total	206	20	9.7	148	71.9	5	2.4	24	11.6	9	4.4

* From Ott.[1]

Each of the six categories of the causes of maternal deaths was further analyzed as to the detailed cause of death. In the category of hemorrhage, it was found that postpartum uterine atony accounted for 19 deaths, ruptured uterus for 17, and ruptured ectopic pregnancy for 13. Other hemorrhage deaths were due to such causes as abruptio placentae, placenta previa, and laceration of the cervix. In the cardiovascular category, rheumatic heart disease was found to be the cause of 20 deaths, hypertensive cardiovascular disease of 11, vascular pulmonary embolus of 6, and amniotic fluid embolism of 3. In the toxemia category, eclampsia caused 20 deaths, preeclampsia 5, hypertension 5, and chronic nephritis 1. Infection following cesarean section accounted for nine deaths; infection associated with abortion was the specific cause of seven deaths; postpartum (unspecified) infections accounted for four; and infections associated with ectopic pregnancy accounted for three deaths. In the anesthesia category, spinal anesthesia accounted for six deaths, inhalation anesthesia for five, and caudal for one. The miscellaneous causes included electrolyte imbalance in five cases; incompatible blood transfusion in two; hepatitis, air embolism, potassium permanganate poisoning, and chorioepithelioma for one each. This detailed classification of causes of death was further correlated with the major responsibility as assigned to the patient, the physician, or the hospital as well as with whether the preventable factors were undeterminable and whether the death was not preventable.

Table 5.—*Distribution of Maternal Deaths with Regard to Preventability Factors, 1954-1955**

Cause	No.	Preventable	Not Preventable	Not Determined
Hemorrhage	8	6	1	1
Toxemia	8	7	..	1
Cardiovascular	7	3	4	..
Infection	3	2	..	1
Anesthesia	2	1	..	1
Other	3	2	..	1
Total	31	21(67.7%)	5(16.1%)	5(16.1%)

* From Longyear, table, p. 10, with modifications.[2]

The nonrelated, nonobstetric deaths were also analyzed. They included the communicable diseases; infectious diseases; such infections as pyelonephritis; such cardiac diseases as hypertensive and rheumatic heart disease; vascular disease, such as cerebral hemorrhage and thrombosis, that was not considered as the result of pregnancy complications; hemorrhages, such as those from a duodenal ulcer; blood dyscrasias; various malignancies; and others. Even though these nonrelated, nonobstetric deaths were relatively unimportant, the committee did determine preventability factors and assign responsibility in all cases possible. It is interesting to note that in this group of 49 deaths, 37 were classified as not preventable, 7 were classified as preventable with the major responsibility that of the physician, 3 were classified as preventable with the major responsibility that of the patient, and 2 were undeterminable.

Table 6.—*Maternal Deaths, Preventability and Responsibility, 1954-1955**

			Responsibility					
			Patient		Physician		Hospital	
Cause	No.	Preventable	Full	Partial	Full	Partial	Full	Partial
Hemorrhage	8	6		3	1	5		5
Toxemia	8	7		3	1	5		3
Cardiovascular	7	3	1		1	2		2
Infection	3	2	1		1			
Anesthesia	2	1			1			
Other	3	2	2					
Total	31	21	4(12.9%)	6	5(16%)	12		10

* From Longyear, table, p. 10, with modifications.[2]

An analysis of the last three years of the study are in the process of compilation at this time. Tables 5 and 6 represent a partial analysis for the 1954-1955 fiscal year. Of 31 maternal deaths, 21, or 67.7%, were considered preventable, with hemorrhage and toxemia leading the list of causes. The patient was believed fully responsible in 12.9% of the cases and the physician in 16% (table 6). In 38.6% of the preventable deaths, responsibility was assigned partially to physician, patient, and hospital in various combinations. In the deaths assigned either partially or fully to the responsibility of the physician, the factor of greatest incidence was failure on the physician's part to recognize or to evaluate properly evidence of complications; inadequate treatment of complications, failure to obtain consultation, and inappropriate choice of procedure or drug followed as factors of decreasing numerical importance. The committee found that inadequate facilities and lack of accepted professional standards were the preventable factors assigned as the responsibility of the hospital. Delay in obtaining medical care was the most frequent factor in patient responsibility, while failure to follow the instructions of the physician and self-induced abortion or injection of injurious drugs were also factors of importance.

Comments and Conclusions.—Since 1941, except for a three-year interruption during World War II, the Maternal Welfare Committee of the Wayne County Medical Society has conducted a continuous study of maternal deaths in Detroit. Various methods of operation have been tried, and ways and means for making the study as effective as possible have been explored. From time to time, various techniques have been incorporated in the study. In 1949, open committee meetings were inaugurated. All members of the profession, including medical students, interns, and residents, were invited to attend. Because the attending physician did not often respond to a separate letter of invitation to the meeting at which his case was to be discussed, the committee obtained permission from the council of the Wayne County Medical Society to send a letter to each attending physician who has had a case discussed by the committee. This letter contains the detailed findings and recommendations resulting from a complete analysis of the particular case in question. Since 1953, in addition to sending the letter to the attending physician, the committee has been sending a similar letter to the hospital administrator and to the chief of staff of the hospital in which the death occurred. In 1951 the committee developed uniform case protocols, copies of which are sent, before each meeting, to the physicians whose cases are being discussed, to all members of the committee, and to the obstetric departments of the hospitals in Wayne County. In 1951 an internist and a pathologist were added to the committee, and since 1954 the membership has included an anesthesiologist.

Since 1950, an obstetric consultation program has been sponsored by the committee. This is a volunteer program, with specialists on the committee agreeing to serve. Consultation is given without fee for indigent cases in hospitals not having obstetric specialists on their medical staff. In addition, the Detroit Department of Health, in cooperation with the committee, has established prenatal lectures as well as clinic service for patients of the lower economic groups who are often not hospitalized. Effective dissemination of specialized information to the busy practitioner has always been a problem. In an effort to help alleviate this, the committee is promoting the publication of articles designed to present recent advances in obstetrics. These frequently appear in the weekly *Detroit Medical News.*

Through the medium of its open meetings, the committee has endeavored to have cases presented over certain periods of time that would emphasize the varied aspects of recurrent complications encountered in its study. By a concentration of discussions on certain problems and complications that occur frequently, the committee has been able to establish mutually acceptable standards of management of such cases. Also, when cases of maternal death are reviewed that illustrate relatively rare problems, the committee has endeavored to obtain discussions on these particular problems by physicians who have particular interest in, or information on, these complications. In these and other ways, the committee is always planning for more proficiency and effectiveness in its study of maternal deaths.

Recently, the Maternal Welfare Committee has recommended that a subcommittee or board of review be established to examine all case material available, determine those cases that are most suitable for discussion, and, in cases where information is not complete, request such additional data as the board of review feels is necessary. In this way, then, it is anticipated that the committee study will contribute more valuable data to the current postgraduate educational program. The proposed board or subcommittee would also review and classify at interim meetings all cases that are not presented for review at the regular monthly open meetings.

In conclusion, the philosophy of the Wayne County experience can be summed up in two quotations by a former chairman of the Maternal Welfare Committee. He points out that "Critical reviews of maternal deaths have become essential in determining what are the current problems in obstetric practice. Their evaluation is necessary to discover our professional shortcomings."[3] He states in his committee report for 1953-1954 that "Preventability and responsibility of the maternal deaths studied are designated as a means of determining areas of currently significant obstetrical problems for which effective solutions are needed. . . . It is the conviction of the Committee that only by honestly recognizing the existing problems and by sincerely attempting to find satisfactory answers can true professional progress be maintained."[4]

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1. Ott, H. A.: Tables and Data by Chairman of Maternal Welfare Committee, 1951-1954, presented before Michigan Society of Obstetricians and Gynecologists, Detroit, Feb., 1955.

2. Longyear, H. N.: Committee Reports—1954-55, Maternal Welfare Committee, Detroit Med. News **47:** 10 (June 27) 1955.

3. Ott, H. A.: Foibles and Pitfalls in Obstetric Hemorrhage, Minnesota Med. **38:** 685 (Oct.) 1955.

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MEDICAL NEWS

ARIZONA

Cancer Seminar in Phoenix.—The American Cancer society, Arizona division, will hold its 1957 cancer seminar, Jan. 10-12, 1957, at the Paradise Inn in Phoenix. Dr. Edward H. Bregman, Phoenix, president of the division, will serve as chairman and Dr. James D. Barger, Phoenix, as co-chairman. Credit for attendance will be given by the Academy of General Practice. Out-of-state speakers will include Drs. Joseph W. Gale and John Z. Bowers, Madison, Wis.; Leo H. Garland and David A. Wood, president, American Cancer Society, San Francisco; David C. Dahlin, Rochester, Minn.; J. Vernon Luck, Los Angeles; Eugene P. Pendergrass, Philadelphia; Hans G. Schlumberger, Columbus, Ohio; Dominic A. DeSanto, San Diego, Calif.; Joe V. Meigs, Boston; and Alfred A. Gellhorn, New York. For registration, write to Arizona Division, American Cancer Society, 1429 N. 1st St., Phoenix.

ILLINOIS

Personal.—Col. Roland I. Pritikin, M. C., U. S. Army Reserve, Rockford, recently returned from the International Congress of the History of Science, Florence, Italy, where he spoke on "History of Treatment of Congenital and Hereditary Eye Defects" and "History of the Introduction to the Management of Mass Eye Casualties Resulting from Radiation Trauma."

Chicago

Lectures on the Growth of Medicine.—Northwestern University Medical School will present the 1957 lectures in "The Growth of Medicine," Tuesdays, 5-6 p. m., in room 641 of the Ward Memorial Bldg., 303 E. Chicago Ave. The January schedule includes the following lectures:

Jan. 8, Barry J. Anson, Ph.D., professor of anatomy, The Debt of Medicine to Ancient Greece and Rome.
Jan. 15, Frederick Stenn, associate professor of medicine, The Medicine of Primitive and Ancient Man.
Jan. 22, Raymond W. McNealy, associate professor of surgery, emeritus, The Influence of the Cook County Hospital on Medical Education in the United States.
Jan. 29, Benjamin Boshes, professor of nervous diseases, The Development of Our Knowledge of Psychiatry.

Lectures on History of Surgery.—On Tuesday, Jan. 8, 1957, at 8 p. m. the International College of Surgeons will present "Early French Surgery" by Dr. G. Kasten Tallmadge, professor of the history of medicine, Marquette University School of Medicine, Milwaukee. All physicians are welcome to attend the lecture, which will be given at the Surgeons' Hall of Fame, 1524 Lake Shore Dr.

Course in Radiation Physics.—The annual course in radiation physics and the James T. Case Lectures for residents in radiology at the hospitals associated with Northwestern University Medical School will be open to all interested physicians (Monday and Thursday, 6:45-9 p. m., Jan. 7–May 7, 1957, in the Morton Research Building, 303 Chicago Ave.). For further information write to the Director, Graduate Division, Northwestern University Medical School, 303 E. Chicago Ave., Chicago 11.

University News.—Dr. William M. S. Ironside of the Royal Infirmary, Edinburgh, Scotland, has been appointed assistant professor of otolaryngology in the department of surgery at the University of Chicago School of Medicine. Dr. Ironside served as a fellow and instructor in otolaryngology at the university for the year ending July 31, 1955. Mrs. Ironside is also a physician.——Dr. John F. Kramer, formerly on the faculty of the Yale University School of Medicine, New Haven, Conn., has been named associate professor of psychiatry at the University of Chicago School of Medicine. Dr. Kramer has been affiliated with Children's Hospital, Los Angeles; the Alfred I. Dupont Institute, Wilmington, Del.; Child Development Institute, New York Hospital; and the Rochester (N. Y.) Child Health Institute.——Dr. William A. J. Crane, lecturer in pathology at the University of Glasgow, Scotland, has joined the staff of the Ben May Laboratory of Cancer Research at the University of Chicago School of Medicine. Dr. Crane is a member of the Scottish Society of Experimental Medicine, the Pathological Society of Great Britain and Ireland, the Royal Medical Society of Glasgow, and the British Medical Association.——Dr. John T. Grayhack has been named director of a new laboratory for research in urology at Northwestern University Medical School. The laboratory was made possible by the Lucy and Edwin Kretschmer Fund, created in honor of his wife and son by the late Dr. Herman L. Kretschmer, a past-president and treasurer of the American Medical Association and a Northwestern alumnus, who died in 1951.——Northwestern University Medical School announces the appointment of Dr. Zachary Felsher, formerly on the faculties of the University of Chicago and the University of Illinois, as assistant professor in dermatology; Dr. Frank J. Fara, chief of obstetrics and gynecology at St. Anthony de Padua Hospital in Chicago and at MacNeal Memorial Hospital in Berwyn, as assistant professor in obstetrics and gynecology; and Dr. Harold Koenig, chief, department of neurology, Veterans Administration Research Hospital at the Northwestern Medical Center, as assistant professor in neurology and psychiatry.——Dr. Chi Kong Liu has been promoted to clinical associate in medicine at Chicago Medical School. Dr. Liu, a native of Canton, China, received his medical degree at National Central University in Nanking, completed his internship and residency in China, and entered Stanford University School of Medicine, Stanford University—San Francisco, for postgraduate studies, serving as a fellow in medicine and a fellow in cardiology. Dr. Liu is co-author of a new book on cardiac pressures and pulses with Dr. Aldo A. Luisada, head of the department of cardiology at Chicago Medical School.

MASSACHUSETTS

Meeting on Gastroenterology.—The Boston Gastroenterological Society (Dr. John J. Byrne, president) will hold a dinner meeting for members and guests, Jan. 9, 1957, 6:30 p. m. "Diseases of the Pancreas" will be the subject of a panel discussion in which "Cancer of the Pancreas" will be presented by Dr. Charles G. Child III, professor of surgery, Tufts College Medical School; "Acute Pancreatitis" by Dr. Perry J. Culver, associate in medicine, Harvard Medical School; "Laboratory Aids in the Diagnosis of Pancreatic Disease" by Dr. Franz J. Ingelfinger, associate professor of medicine, Boston University School of Medicine; and "Surgery of the Sequelae of Pancreatitis" by Dr. Kenneth W. Warren, department of surgery, Lahey Clinic.

MISSOURI

Hanau Loeb Lecture.—The Alpha Pi chapter of Phi Delta Epsilon fraternity at the St. Louis University School of Medicine will hold its 12th annual Hanau W. Loeb Lectureship Jan. 8, 1957, at 5 p. m. The guest speaker, Dr. Shields Warren, Harvard Medical School, Boston, will discuss "Man and His Atomic Environment." Dr. Warren is the former director of the division of biology and medicine, U. S. Atomic Energy Commission.

NEW YORK

Society News.—At a meeting of the Westchester chapter, American Federation for Clinical Research, Nov. 15, at the Nurses' Auditorium, White Plains Hospital, Dr. Charles Weller Jr., Larchmont, presented "The Oral Anti-Diabetic Compounds" and Drs. John J. Kneisel, White Plains, and O. Alan Rose, New York City, presented "Two Cases of Diencephalic Syndrome, One Treated with Splanchnicectomy and One with Reserpine."

Pilot Project in Mental Hygiene Institutions.—A program to increase volunteer services in the state's mental hygiene institutions was inaugurated in August with the appointment of a statewide director of volunteers, Miss Barbara Griffiths, former director of volunteers at Hudson River State Hospital. According

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

to Dr. Paul H. Hoch, commissioner of mental hygiene, the effect of a volunteer program on hospital-community relationships was successfully proved in the experimental project at the Hudson River State Hospital. As a first step in the new program, Miss Griffiths will survey the needs and the ability to meet these needs in each of the state's 27 institutions and the community it serves. The expanded volunteer program is being initiated under a grant obtained from the Doris Duke Foundation, New York City, by the New York State Society for Mental Health.

Hospital News.—Grants of $256,400 for research and nonoperating purposes at Hillside Hospital, Glen Oaks, L. I., were recently announced by Dr. Joseph S. A. Miller, medical director. Hillside is a nonprofit mental hospital affiliated with the Federation of Jewish Philanthropies.——The Salvation Army announces the appointment of Drs. Samuel D. Blum, New York City, and Ancel U. Blaustein, Hollis, L. I., to the staff of the new Booth Memorial Hospital in Queens. Dr. Blum is a clinical professor and Dr. Blaustein is assistant professor of pathology at the New York Medical College, Flower and Fifth Avenue Hospitals. Booth Memorial Hospital (North Hempstead Turnpike and Main Street, Flushing) was scheduled to be completed in December. The 200-bed institution will provide general care for middle-income families, facilities for the study of geriatrics, and the continuation of the program for unmarried mothers.

University News.—Dr. Kwang Soo Lee, associate professor of pharmacology, Jefferson Medical College of Philadelphia, has been appointed associate professor of pharmacology at the State University of New York College of Medicine at New York City, Brooklyn. Dr. Lee holds the degrees of M.D. and Ph.D. in pharmacology from Keijo Imperial University, Japan, and of Ph.D. in biochemistry from Johns Hopkins University, Baltimore.——Albany Medical College announces the formation of a department of microbiology, an outgrowth of the departments of bacteriology and pathology. Scott V. Covert, Ph.D., has been named professor and chairman of the new department, which will have the primary duty of conducting microscopic studies of bacteria, viruses, fungi, and parasites in relation to infectious diseases. His staff will also assist in the training of medical technologists at Albany Hospital and in the teaching of nurses at the Albany Medical Center School of Nursing.——Dr. Douglass S. Thompson, clinical instructor in medicine at New York University College of Medicine, was named university physician, to succeed Dr. John E. Sawhill, who retired after 32 years of service. Dr. Thompson has served as New York University intern and resident at Bellevue Hospital and, since 1953, as an assistant in medicine at the college of medicine. For the last two years he also has been a U. S. Public Health Service trainee at Bellevue. Dr. Thompson is secretary of subsidiary board A of the National Board of Medical Examiners, New York City, and a member of the research committee of the American College Health Association.

New York City

Dr. Graef Honored.—Dr. Irving P. Graef, who has been a leader in the work of the National Committee for Resettlement of Foreign Physicians (31 Union Sq. W.) since its organization in 1939, was honored Nov. 5 as the retiring chairman of the board of directors "for his distinguished efforts in helping foreign physicians reestablish themselves in their profession in the United States." He was presented with a bronze plaque and two volumes of letters of appreciation at a luncheon in his honor at the New York Academy of Medicine. Dr. Graef will remain national vice-chairman of the committee. Dr. Robert Boggs, former dean of the New York University Post-Graduate Medical School, is the new chairman of the board. Dr. Graef has served as secretary-treasurer of the Society of Experimental Biology and is associate editor of *Diabetes——The Journal of the American Diabetes Association*. He is a member of the board of directors of National Medical Fellowships, which provide money for Negro medical students for postgraduate study in medical schools.

Personal.—Dr. Abraham Kardiner, clinical professor of psychiatry, Columbia University College of Physicians and Surgeons, recently addressed the Long Island Psychiatric Society at its meeting at the Veterans Administration Hospital, Northport, on "Social Conditions Under Which Psychiatry Arose and Can Survive."——Dr. Maurice L. Tainter, director of the Sterling-Winthrop Research Institute in Rensselaer, has been elected a trustee of Albany Medical College. He is a past-president of the New York Academy of Sciences, and formerly was head, department of physiological sciences, Stanford University in California.——Dr. Maxwell L. Littman, research associate, department of microbiology, Mount Sinai Hospital, was elected chairman of the division of mycology of the New York Academy of Sciences for the 1957 term. He is co-author of "Cryptococcosis-Torulosis" with Dr. Lorenz E. Zimmerman of the Armed Forces Institute of Pathology, Washington, D. C.——Dr. Francis S. Caliva, assistant professor of medicine, State University of New York College of Medicine, Syracuse, has been appointed medical director of the Syracuse Dispensary, 601 E. Fayette St., succeeding Dr. Richardson K. Noback, who resigned to become affiliated with the University of Kentucky College of Medicine, Louisville.——Dr. Bernard Kalfayan has been appointed director of laboratories at the Roosevelt Hospital. Born in Turkey and now a naturalized American citizen, Dr. Kalfayan was graduated from the American University of Beirut, School of Medicine, Lebanon. He has served as assistant professor of pathology at Cornell University Medical College, associate attending pathologist at New York Hospital, associate pathologist at Roosevelt Hospital, and director of laboratories of Beekman-Downtown Hospital.

OREGON

Personal.—Dr. Howard P. Lewis, professor of medicine, University of Oregon Medical School, Portland, has been appointed to the National Advisory Heart Council, according to an announcement by the surgeon general of the Public Health Service.

Professor of Obstetrics and Gynecology.—Dr. Ralph C. Benson, San Francisco, has been appointed as professor and as the first full-time head of the department of obstetrics and gynecology at the University of Oregon Medical School, Portland. Dr Benson previously served as associate professor of obstetrics and gynecology at the University of California Medical School, San Francisco. Dr. Howard C. Stearns, Portland, who has been a faculty member since 1932 and clinical professor and head of the department since 1945, will continue as clinical professor and will assume the post of senior consultant.

TENNESSEE

Course on Diseases of the Chest.—A course on diseases of the chest will be sponsored by the council on postgraduate medical education of the American College of Chest Physicians with the cooperation of the southern chapter of the college and the Vanderbilt University School of Medicine, Nashville, at the school of medicine, Jan. 14-19, 1957. The tuition fee, $75, includes five luncheons. Out-of-state participants will include Drs J. Winthrop Peabody, Washington, D. C., Gerritt W. H. Schepers, Saranac Lake, N. Y.; M. Jay Flipse, Miami, Fla.; Alvis E Greer, Houston, Texas; Osler A. Abbott, Emory University, Ga., Lawrence H. Strug, New Orleans, John S. Harter, Louisville, Ky.; and Robert P. Glover, Philadelphia. Forty-two hours of informal credit will be allowed by the Academy of General Practice. Applications may be sent to the American College of Chest Physicians, 112 E. Chestnut St., Chicago 11.

WASHINGTON

Professor of Pediatrics.—Dr. Robert A. Aldrich, associate professor of pediatrics at the University of Oregon Medical School, Portland, has been appointed by the University of Washington School of Medicine, Seattle, as head of the department of pediatrics. Dr. Aldrich previously served as a resident for three years at the University of Minnesota Hospital, Minneapolis, and an associate and consultant in pediatrics at the Mayo Clinic, Rochester, Minn. He succeeds Dr. Walter B. Seelye, who has been forced to limit his activity because of illness.

Health Officers Needed.—The Washington State Personnel Board (212 General Administration Bldg., Olympia) announces that applications will be accepted until further notice for (1) district health officer (salary, $864 to $1,032) and (2) medical health officer (salary, $692 to $826). Applicants must be graduates of an approved school of medicine, including or supplemented by a one-year rotating internship. In addition, district health officer applicants must have completed one year of graduate training in public health and must have had (1) at least two years of successful full-time experience in public health work; or (2) approved public health residency training, which may be substituted year for year for the required experience; or (3) three years of successful, full-time, professional medical practice. A license to practice medicine in the state of Washington must be acquired before probationary appointment or at the first meeting of the board of medical examiners after such appointment. Residence in the state is not required before appointment. A recent photograph should accompany application.

WEST VIRGINIA

Cancer Registry.—A central cancer registry, under the joint sponsorship of the state department of health and the West Virginia Cancer Society, will be available on and after Jan. 1, 1957. The registry will be housed with the state department of health, and the personnel will be associated closely with the divisions of cancer control and vital statistics. The central registry, which initially will have the cooperation of at least 11 hospitals, will provide a systematic follow-up of all cancer patients and keep them under adequate lifetime medical observation.

GENERAL

Course on Radiologic Safety.—A full-time course in radiologic safety will be given Jan. 7-18, 1957, by the New York University Post-Graduate Medical School in cooperation with the U. S. Atomic Energy Commission. The course is designed for physicians, engineers, and persons in research laboratories. For the convenience of those who cannot take the course full time, it will be repeated on a part-time basis from Jan. 30 to May 22. There will also be an optional laboratory session from Jan. 21 to Feb. 1. For information, write to the Dean, Post-Graduate Medical School, 550 First Ave., New York 16.

Seminars on Thyroid-Uptake Measurement.—The medical division of the Oak Ridge (Tenn.) Institute of Nuclear Studies will present six thyroid-uptake seminars this winter and spring, to provide instruction in a standard method of calibrating the uptake of radioiodine by the thyroid. Seminars A and B (Jan. 14-15 and Feb. 11-12, 1957) will be limited to participants in the Oak Ridge survey of thyroid-uptake measurement. Seminars 1 and 2 (March 18-19 and April 15-16) will be open to a limited number of qualified physicians and physicists who have not participated in the institute's thyroid-uptake calibration survey. The fee will be $25. Seminar 3 (May 17) will be open only to representatives of manufacturers of thyroid-uptake equipment. A maximum of 60 participants will be accepted, and a $25 fee will be charged. Seminar 4 (June 10-14) will accommodate a total of 30 technicians employed under the direction of physicians who have attended one of the previous seminars. This experimental seminar will train technical assistants for work with professional staff members. A fee of $25 per person will be charged. Information concerning any of the seminars, and application forms may be obtained by writing Mr. William Busby, Oak Ridge Institute of Nuclear Studies, Medical Division, P. O. Box 117, Oak Ridge, Tenn.

Industrial Accidents Decrease.—The National Safety Council (425 N. Michigan Ave., Chicago 11) reports that industrial injury rates for 1955 showed a reduction in frequency and an increase in severity compared with those of 1954. Of the 40 basic industry classifications, 25 reduced their frequency rates. Although more than half reduced their severity, this reduction did not make up for the increases of others. The average accident-frequency rate for employees in all industries submitting company reports to the council, based on the number of disabling injuries per million man-hours, was 6.96 in 1955, a reduction of 4% from the year before. This is the first time that the all-industry rate has been held to less than 7. The lowest employee frequency rate (0.86) was reported by the communications industry. This was a 34% improvement from the 1954 rate, which was also the lowest for all industries. Electrical equipment held second place with a rate of 2.13, a 15% reduction. Aircraft manufacturing and cement made 21% improvements. The average accident severity rate for all industries reporting to the council, based on the number of days lost per million man-hours, was 815 last year—an increase of 2%. Tobacco, with a rate of 87 and a 1955 reduction of 59%, was first in the severity column; communications was second, with a rate of 97; and service industries third, with a rate of 105.

Foundation for Eye Care.—The National Medical Foundation for Eye Care, a nonprofit scientific and educational institution, has been incorporated in New Jersey, "to provide American ophthalmology with an agency to present to the public generally and to fellow physicians pertinent information on the care and treatment of the eyes." Dr. Ralph O. Rychener, Memphis, Tenn., is president of the foundation; Dr. Edwin F. Tait, Norristown, Pa., vice-president; and Dr. Charles E. Jaeckle, East Orange, N. J., secretary-treasurer. Other members of the board of trustees are Drs. Alson E. Braley, Iowa City; Frederick C. Cordes, San Francisco; Paul A. Chandler, Boston; J. Spencer Dryden, Washington, D. C.; Harold F. Falls, Ann Arbor, Mich.; Everett L. Goar, Houston, Texas; Erling W. Hansen, Minneapolis; Albert D. Ruedemann, Detroit; Barnet R. Sakler, Cincinnati; and Derrick T. Vail, Chicago. The foundation invites all ophthalmologists and other physicians in eye care to become charter members. Applications are available through Dr. Charles E. Jaeckle, secretary-treasurer, at 136 Evergreen Pl., East Orange, N. J. The foundation will establish an administrative office in New York City about Jan. 1, 1957, and will also make available an affiliate membership for persons other than doctors of medicine who are interested in aiding the purposes of the foundation.

Society News.—Newly elected officers of the American Association of Neuropathologists include: Dr. Ben W. Lichtenstein, Chicago, president; Dr. Konstantin Scharenberg, Ann Arbor, Mich., vice-president; and Dr. Leon Roizin, New York, secretary-treasurer.——Newly elected officers of the New England Roentgen Ray Society include: Dr. Leslie K. Sycamore, Hanover, N. H., president; Dr. Harvey R. Morrison, Boston, vice-president; Dr. Raymond A. Dillon, Winchester, secretary; and Dr. Magnus I. Smedal, Boston, treasurer.——Officers of the Medical Library Association include Miss Bertha B. Hallam, Portland, Ore., president; Mrs. Henrietta T. Perkins, New Haven, Conn., secretary; Miss Pauline Duffield, Austin, Texas, treasurer; and Mr. Thomas E. Keys, Rochester, Minn., president-elect.——The American Board of Legal Medicine recently elected the following officers: Dr. Alfred Koerner, New York City, president; Dr. Harold Lefkoe, Philadelphia, vice-president; Dr. Sidney I. Franklin, Youngstown, Ohio, second vice-president; Dr. Harold M. Pritchard, Niles, Mich., third vice-president; Dr. Maxwell M. Booxbaum, Bronxville, N. Y., secretary; Dr. Louis J. Gelber, Rockville Centre, N. Y., assistant secretary; Dr. Israel Bernard Malkin, Brooklyn, N. Y., treasurer; and Dr. Ewing H. Crawfis, Little Rock, Ark., assistant treasurer. The board's 1957 convention will be held in New York City immediately preceding the A. M. A. convention.

Fund for Psychiatry.—The American Fund for Psychiatry (organized in 1954) announces fellowship awards for 1956, totaling $30,000, to the following medical schools and other training institutions to support teaching appointments of these young physicians:

John A. MacLeod, department of psychiatry of the University of Cincinnati College of Medicine, second year grant.
Virgilio G. Santiago, Hahnemann Medical College and Hospital of Philadelphia.
Francis H. Hoffman, Temple University School of Medicine, Philadelphia, second year grant.
Bernard P. Ottenberg, University of Pennsylvania School of Medicine, Philadelphia.
Thomas S. Szasz, Institute for Psychoanalysis, Chicago.

The fund raises money from corporations, foundations, and individuals for the purpose of financing academic and research appointments in psychiatry. Its aim is to reduce the critical shortage of teachers and researchers in the mental health field. The awards were made by a committee of physicians under the chairmanship of Dr. Vernon W. Lippard, dean of the Yale University School of Medicine, New Haven, Conn. In the two years of its existence the fund has made specific grants and fellowship awards in support of psychiatric research and training totaling $75,000. It is currently engaged in a campaign to raise $250,000 for 1956 to finance future research grants and fellowships.

Outbreaks of Encephalitis.—In its communicable disease summary for the week ended Sept. 22, the National Office of Vital Statistics of the U. S. Public Health Service says that Dr. Roy F. Feemster, Massachusetts Department of Public Health, Boston, has reported another suspected human case of eastern equine encephalitis that proved to be fatal. The total for the year is now 12 affected persons, of whom 7 have died. Virus has been isolated in four fatal cases, and serologic evidence of infection has been found in three of the survivors. A total of 38 cases in horses has been reported, from which 6 virus isolations have been made, and a high antibody titer was found in one surviving animal. Two virus isolations have been made from pheasants on pheasant farms. A recent confirmed case in a horse was found in Southbridge near the Connecticut border. Infection in pheasants on farms, confirmed by virus isolation, has been found in nearby areas of Connecticut.

In other areas, human cases of arthropod-borne types of encephalitis have been found as follows: three suspected human cases of eastern equine infection in New Jersey and two in Louisiana are being investigated. Serological evidence of St. Louis encephalitis has been found in one case in California and one in Colorado. There are 12 cases in Colorado in which the presumptive diagnosis is of the St. Louis type of infection. California has reported eight cases of western equine encephalitis for which there is serologic evidence of infection. Of 850 pools of mosquitoes received for testing in this state, western equine virus has been isolated from 124; tests on 372 have revealed negative results, and the remainder are still being tested. A few cases of encephalitis are being investigated in western Kansas, not far from an area in Texas where cases are also reported to be occurring. Eight suspect cases, with one death, from western equine encephalitis reported in the state of Washington in July, were still under investigation. Two cases with one death had occurred in Idaho, but neither had been confirmed.

Mine Workers Welfare and Retirement Fund.—The annual report of the United Mine Workers of America Welfare and Retirement Fund, released Sept. 6, highlights the 10th anniversary of the fund's operations. Benefits paid during this decade totaled $880,819,489.10 and aided 972,004 beneficiaries—miners, their families, their widows and orphans. Revenues received during the 10-year period totaled $1,036,650,955.03. The fund is organized and administered as a separate entity, independent of the union and the coal operators, by its three trustees, John L. Lewis, chairman and chief executive officer, Charles A. Owen, and Josephine Roche.

The annual report shows that on June 30, 1956, there were 61,546 retired miners receiving the $100 monthly pensions, in addition to federal Social Security or other income the miner may enjoy. The average age of these pensioned miners at retirement was 63.8, and they had worked an average of 32.3 years in the coal industry. The annual report further shows that funeral expenses and widows' and survivors' benefits of $3,190,358.94 aided 7,320 widows, orphans, and other survivors of deceased miners. Additional payments of $69,807 in mine disaster benefits aided the families of 241 miners killed or seriously injured in mine disasters during the year.

A major development during the past fiscal year in the medical and hospital program, under the direction of Dr. Warren F. Draper, Washington, D. C., executive medical officer of the fund, was the opening of a network of 10 hospitals operated by the Miners Memorial Hospital Association (see The Journal, March 27, 1954, pages 1101-1103). The fund's unexpended balance as of June 30, 1956, was $130,172,370.58, an increase of more than 26 million dollars over the previous fiscal year. The total revenues for the year were $154,227,174.35, the total expenditures were $127,662,715.10, of which 97.1% were payments aiding 206,919 beneficiaries. All administrative costs of the fund, including those of its Washington headquarters and its 10 area medical offices, were 2.9% of the total fund expenditures.

FOREIGN

Personal.—Sir Russell W. E. Brain, Bt., president of the Royal College of Physicians, has accepted appointment as a trustee of the Ciba Foundation, an organization dedicated to the promotion of international cooperation in medical and chemical research.

Postgraduate Courses in Austria and Switzerland.—The West German Federation of Physicians' Councils has scheduled a continuation school for medical practitioners, at which the general subject will be "Sulfonamide, Antibiotica and Cortisone." Parallel courses will be given March 11-23, 1957, at Bad Gastein, Austria, and at Davos, Switzerland. The official language of the conventions will be German. Information may be obtained from Wolfgang Brune at the federation's headquarters, Haedenkampstrasse 1, Koln-Lindenthal, Germany.

Training Program in Urology.—The first training program in Urology to be given in India will be set up by Dr. Roger W. Barnes, chairman of the department of urology at the College of Medical Evangelists, Loma Linda, Los Angeles, who left July 1 for Vellore, India, where he will remain until next summer. The program will be established at the Christian Medical College, where Dr. Barnes will also lecture in urology under a Fulbright award.

EXAMINATIONS AND LICENSURE

American Board of Anesthesiology. *Part I.* Various locations, July 19 Final date for filing application is Jan. 19. *Oral* Asheville, No Car, Mar 24-29. Sec., Dr. Curtiss B. Hickcox, 80 Seymour St., Hartford 15, Conn

American Board of Dermatology. *Written.* Several cities, June 27 *Oral.* Baltimore, Oct. 11-13. Sec., Dr. Beatrice Maher Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *Written* Oct. 21. *Oral* New Orleans, Feb. 4-8; Boston, April 3-6. Final date for filing application is Jan. 2. Chicago, May 27-29, San Francisco or Los Angeles, September Final date for filing application is Feb 1. *Subspecialties Gastroenterology* Philadelphia, April 5-6. Final date for filing application is March 1 Exec Sec., Dr. W. A. Werrell, 1 West Main St., Madison 3, Wis

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

American Board of Obstetrics and Gynecology. *Part I* Various cities of the United States, Canada, and military centers outside the Continental United States, Feb. 1. Candidates must submit case reports to the office of the Secretary within thirty days of being notified of their eligibility to Part I. The cases must be *prepared in the manner* described in the Bulletin of the board with a duplicate index list. *Part II.* Chicago, May 16-25 Request for reexamination in Part II must be received prior to Feb 1 Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6, Ohio

American Board of Ophthalmology· *Written.* Jan 21. Final date for *filing application* was July 1. *Oral* New York, May 23-27, Chicago Oct. 7-11. *Sec.*, Dr. Merrill J. King, Box 236, Cape Cottage Branch *Portland* 9, Maine.

American Board of Orthopaedic Surgery. *Oral Part II* Chicago, January 1957. Final date for filing application was Aug. 15 Sec, Dr Sam W. Banks, 116 South Michigan Ave, Chicago 3.

American Board of Otolaryngology. Chicago, Oct 7-11. Final date for filing application is April. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pathology. *Oral and Written Pathologic Anatomy and Clinical Pathology* Washington, April 4-6. Final date for filing application is March 1. Sec., Dr. Edward B. Smith, 1040 West Michigan St, Indianapolis 5

American Board of Physical Medicine and Rehabilitation *Parts I and II.* New York City, June 8-9. Final date for filing application is March 1. Sec., Dr. Earl C. Elkins, 200 First St., S W., *Rochester*, Minn

American Board of Plastic Surgery. *Entire Examination* Philadelphia, May 4-6. Final date for filing case reports is Jan 1 Corres Sec, Mrs Estelle E. Hillerich, 4647 Pershing Ave, St. Louis 8

American Board of Preventive Medicine. *Oral and Written Public Health.* Schools of Public Health, April 11-13. *Aviation Medicine* Denver, May 9-11. *Occupational Medicine St. Louis, April* 26-28 Sec, Dr Thomas F. Whayne, 615 North Wolfe St., Baltimore

American Board of Proctology. *Oral and Written Parts I and II* September. Sec., Dr. Stuart T. Ross, 520 Franklin Ave, Garden City, N. Y.

American Board of Psychiatry and Neurology *Oral* New Orleans, Mar. 18-19. Final date for filing application was Sept. 10. Sec, Dr David A. Boyd, Jr., 102-110 Second Ave., S.W., Rochester, Minn

American Board of Radiology. Tampa, April 1-6 Final date for filing application is Jan. 1. Washington, Sept. 23-28 Final date for filing application is June 1. Sec., Dr. B. R. Kirklin, Kahler Hotel Bldg, *Rochester*, Minn

American Board of Surgery: *Part II.* Los Angeles, Jan. 14-15, San Francisco, Jan. 17-18, Houston, Feb. 18-19, Nashville, Mar 11-12, Boston, April 8-9, and New York, June 10-11.

American Board of Urology: February 1957. Sec, Dr William Niles Wishard, 1711 N. Capital Ave, *Indianapolis* 7.

Board of Thoracic Surgery: *Written* Various centers throughout the country, February 1957, and the closing *date for* registration is *Dec* 1, 1956. Sec., Dr. William M. Tuttle, 1151 *Taylor Ave*, Detroit 2

GOVERNMENT SERVICES

AIR FORCE

Air Force to Build Medical Center.—The Air Force has announced that the new 8-million-dollar Aero Medical Center, to be built at Brooks Air Force Base, San Antonio, Texas, will house the School of Aviation Medicine, which has been dividing its operations between Randolph Air Force Base, Texas, and Gunter Air Force Base, Alabama. The center, which is scheduled for completion by the end of 1958, was originally authorized by the 82nd Congress in the fiscal year 1953 military construction program.

The first construction contracts provide for an academic building, a flight medicine laboratory, research laboratory shops, and supporting utilities. Contracts to be awarded for the remainder of the facilities include an altitude building and a research building. Establishment of this aeromedical center will allow the Air Force to conduct more extensive research into the medical aspects of supersonic flight problems and to provide greater aviation medicine teaching facilities than are now available. Emphasis will be placed on developing means of protecting fliers at the high speeds and altitudes that are now encountered or that are expected to be encountered in the future.

Noise Exposure Program.—The U. S. Air Force announces that a hazardous noise exposure program is being established to provide an audiometric examination as a part of the routine physical examination of all military and civilian personnel who enter or terminate service in the Air Force. The provision of this examination, which has already begun at Lackland Air Force Base, Texas, is intended to supply a base line for determining and controlling the effects of exposure to hazardous noise. This Air Force program represents the first step of such broad scope in the study, control, and reduction of hearing damage produced by noise.

Joint Committee on Aviation Pathology.—The Joint Committee on Aviation Pathology established by the Department of Defense, Nov. 14, 1955, held its second scientific session at the Armed Forces Institute of Pathology Nov. 15-16, 1956. This committee consists of representatives of the U. S. Air Force, Army, and Navy, the British Royal Air Force and Navy; the Royal Canadian Air Force, and the Armed Forces Institute of Pathology. Its objectives are to study the pathological reports of fatal aircraft accidents in order to evaluate their possible cause; to observe recurring traumatic lesions that may be preventable; to determine the significance of preexisting subclinical lesions in aircrew personnel; to investigate the possible insidious changes induced by repeated exposure to flight conditions; and to establish a long-range program of collection of such information and rapid dissemination of it to the member services.

The second scientific session was attended by 100 civilian and military personnel, before whom about 20 papers were presented. Col. Frank M. Townsend, M. C., U. S. A. F., was elected chairman of the committee for the coming year, replacing Wing Commander E. Bruce Harvey, R. A. F., who had served as chairman since the committee was established.

New Two-Star General.—Brig. Gen. Olin F. McIlnay has been promoted to the rank of major general by direction of the President. General McIlnay was commissioned a first lieutenant in the Medical Reserve in 1928 and on completion of an internship at Letterman General Hospital, San Francisco, he received a regular commission as first lieutenant Aug.1, 1929. In 1942 he became staff surgeon for the eighth fighter command, which later moved to England. In 1944 he became staff surgeon for the second air division in England. In 1945 he became assistant surgeon for the Air Force training command at Fort Worth, Texas, and in 1948 was appointed surgeon for the air training command. In 1952 he became director of plans and hospitalization in the office of the surgeon general at Air Force headquarters, Washington, D. C. General McIlnay has been awarded the Legion of Merit, the Bronze Star medal, and Croix de Guerre with palm.

VETERANS ADMINISTRATION

Rehabilitation of Chronically Ill Veterans.—Chronically ill and aged veterans, hospitalized 10 to 20 years, are being rehabilitated and discharged from VA hospitals under an advanced concept of long-term patient care. Since the new program became operative about a year ago, 1,159 of the initial group of 4,263 long-term hospital patients have been discharged. Dr. I. J. Cohen, hospitals and clinics director, Veterans Administration, Washington, D. C., said, "A concerted effort is made to rehabilitate these chronically ill veterans sufficiently for them to be returned to their homes, to a foster home, or to other appropriate community facilities. Those for whom this is not possible continue to receive the care and treatment needed in as nearly a home-like atmosphere as it is possible to have in a hospital. The VA program," he added, "is an all-out effort by every branch of the hospital staff to rehabilitate long-term patients so they may achieve the best possible physical condition and maximum self-help, and to provide them with recreational, spiritual, and social activities so as to prevent mental regression and social isolation."

By grouping long-term patients on wards or sections, the hospitals are able to relax the rigid routine necessary on wards for acutely ill patients and to provide personnel especially trained in caring for the chronically ill. All VA general medical and surgical hospitals and some VA tuberculosis hospitals are caring for patients of this type, but 49 hospitals have special wards or sections for long-term patients.

FOOD AND DRUG ADMINISTRATION

Statement on Hoxsey Cancer Treatment.—The following statement was released Nov. 16 by G. P. Larrick, U. S. Commissioner of Food and Drugs.

"For the second time, a Federal court has determined that the Hoxsey medicines for internal cancer are worthless. Yesterday, after a six-week trial in the Federal court at Pittsburgh, the jury returned a verdict that these medicines, in pill form, were illegally offered as an effective treatment for cancer.

"The public should know, however, that this action does not end the menace of this fake treatment. It merely means that half a million of the Hoxsey pills, which were seized shortly after the opening of a second Hoxsey Clinic at Portage, Pa., will now be destroyed. An injunction is being sought to stop further interstate shipment of the pills. We intend to use every legal means within our power to protect consumers from being victimized by this worthless treatment.

"In the meantime it is of the utmost importance that cancer patients and their families, who may be planning to try the Hoxsey treatment either at Dallas, Texas, or Portage, Pa., should acquaint themselves with the facts about it. All such persons are advised to secure a copy of the Public Warning which was issued by the Food and Drug Administration last April [J. A. M. A. **160**: 1423 (April 21) 1956]. They may do this by writing to the Food and Drug Administration, Washington 25, D. C.

"Harry M. Hoxsey has continued to promote his worthless cure for more than 30 years, notwithstanding numerous local and state court actions. Proceedings under the Federal Food, Drug, and Cosmetic Act did not appear possible until a 1948 decision of the Supreme Court interpreting the word "accompanying" in the definition of labeling under the Act. An injunction suit was filed in 1950 and a decree finally issued by the Federal court at Dallas in 1953.

"Over the years thousands of persons have been deceived by the false claims for the Hoxsey liquid medicines and pills. At the Pittsburgh trial there was testimony concerning persons who may have died of cancer as a result of reliance on the Hoxsey treatment instead of seeking competent medical treatment in the early stages of their condition. The Government's evidence showed that alleged 'cured cases' presented by defense attorneys were people who did not have cancer, or who were adequately treated before they went to the Portage clinic, or died of cancer after they had been treated there."

Munford, Samuel Archer, Clifton Springs, N. Y.; born in Princeton, Ind., Dec. 14, 1876; Jefferson Medical College of Philadelphia, 1905; an associate member of the American Medical Association; past-president of the Seventh District of the Medical Society of the State of New York; medical advisor at Cornell University in Ithaca from 1910 to 1917; veteran of World War I; fellow of the American College of Physicians; chief of internal medicine at the Clifton Springs Sanitarium and Clinic from 1919 to 1948, when he became superintendent, serving until 1950; died Oct. 29, aged 79, of hypertensive cardiovascular disease.

Nadel, Samuel, Boston; Tufts College Medical School, Boston, 1920; member of the Massachusetts Medical Society; veteran of World War I; deputy commissioner of health for the city of Boston; for many years school physician; on the staffs of the Allerton Hospital in Brookline and the Harley Private, Boston City, St. Elizabeth's, Carney, and St. Margaret's hospitals; died in the Harley Private Hospital Sept. 10, and 59, of carcinoma of the pancreas.

Naegeli, Frank ⊕ Fergus Falls, Minn.; Northwestern University Medical School, Chicago, 1910; on the staff of the Lake Region Hospital, where he died Oct. 22, aged 82, of myocardial infarction.

Nelson, Frank Arleigh ⊕ Ajo, Ariz.; University of Nebraska College of Medicine, Omaha, 1923; medical superintendent and chief surgeon at the Phelps-Dodge Hospital; died Oct. 28, aged 58, of a heart attack.

Newton, Harlan Fay ⊕ Boston; born in Winchester, Mass., Feb. 8, 1895; Harvard Medical School, Boston, 1920; served on the faculty of his alma mater; member of the founders' group of the Board of Thoracic Surgery and the American Board of Surgery; member of the American Association for Thoracic Surgery; fellow of the American College of Surgeons; at various times on the staffs of the Middlesex County Sanatorium in Waltham, the Burbank Hospital in Fitchburg, and the Peter Bent Brigham Hospital, where he died Oct. 23, aged 61, of acute myocardial infarction.

Notbohm, William R. ⊕ Dousman, Wis.; Milwaukee Medical College, Milwaukee, 1898; for many years president of the Dousman State Bank; died Oct. 23, aged 90, of heart disease.

O'Connor, James Joseph ⊕ Alhambra, Calif.; Loyola University School of Medicine, Chicago, 1931; member of the Indiana State Medical Association; specialist certified by the American Board of Pediatrics; served on the staff of St. Catherine's Hospital in East Chicago, Ind.; died July 2, aged 54, probably of carcinoma of the pancreas and diabetes mellitus.

Rastatter, Paul F., Jackson, Miss.; Baltimore University School of Medicine, Baltimore, 1902; past-president of the Crawford County (Pa.) Medical Society; at one time medical director of Crawford County, Pennsylvania; served on the staffs of the Spencer Hospital in Meadville, Pa.; and St. Vincent's Hospital in Erie, Pa.; died Oct. 12, aged 80, of heart disease.

Ritchey, Billy Fay, Yonkers, N. Y.; State University of Iowa College of Medicine, Iowa City, 1921; served on the staff of the Yonkers General Hospital; formerly medical examiner in the Yonkers public schools; died in the Montefiore Hospital, New York City, Sept. 24, aged 60, of cerebral thrombosis.

Robinson, Edward Percy, Seaside Park, N. J.; Bellevue Hospital Medical College, New York City, 1897; also a pharmacist; died Oct. 13, aged 85, of chronic myocarditis.

Robinson, William Ashby, Old Fort, N. C.; University College of Medicine, Richmond, Va., 1900; served on the staff of the Marion (N. C.) General Hospital; died Aug. 24, aged 78, of heart disease.

Russell, John Colvin ⊕ Detroit; Detroit Homeopathic College, Detroit, 1906; on the staffs of the Grace and North Detroit General hospitals; died in the Mount Carmel Mercy Hospital Sept. 20, aged 77, of carcinomatosis.

Russell, Rosannah, Fort Shaw, Mont.; Northwestern University Woman's Medical School, Chicago, 1900; an associate member of the American Medical Association; died in Great Falls Sept. 27, aged 88.

Schreier, Alexander Rainold, Gillett, Texas; Creighton University School of Medicine, Omaha, 1911; died in the Kenedy Clinic and Hospital in Kenedy Aug. 16, aged 70, of virus pneumonia.

Shepherd, Robert Herbert, Jasper, Ala.; Birmingham Medical College, Birmingham, Ala., 1910; member of the Medical Association of the State of Alabama; died in the Walker County Hospital Sept. 9, aged 70.

Shepherd, Samuel Tinson, Birmingham, Ala.; Atlanta College of Physicians and Surgeons, Atlanta, Ga., 1902; died Sept. 15, aged 80, of carcinoma of the lip with metastasis.

Shultz, Cameron, Danville, Pa.; Jefferson Medical College of Philadelphia, 1892; an associate member of the American Medical Association; served as secretary of the Montour County Medical Society and Danville Board of Health; during World War I medical examiner for the draft board and a member of the Medical Corps of the National Guard; died in the George F. Geisinger Memorial Hospital and Foss Clinic Sept. 19, aged 85, of acute myocardial infarction.

Smith, J. Lewis, Columbia, S. C.; Medical College of the State of South Carolina, Charleston, 1905; for many years surgeon for the Southern Railway; died in the South Carolina Baptist Hospital Sept. 12, aged 74.

Steele, Guy, Cambridge, Md.; University of Maryland School of Medicine, Baltimore, 1897; past-president of the Medical and Chirurgical Faculty of Maryland; served as county health officer, and was associated with the U. S. Public Health Service, for many years on the staff of the Cambridge-Maryland Hospital, where he died Oct. 12, aged 95, of complications following fracture of the hip.

Stieglitz, Leopold, New York City; Universitat Heidelberg Mediziniche Fakultät, Baden, Germany, 1891; an associate member of the American Medical Association; holder of the first medical license issued by New York State; the Leopold Stieglitz visiting professorship was established at the New York University College of Medicine in 1947 by his friends and patients and provides funds for an annual visiting professor to the school, died Oct. 7, aged 89.

Swift, Charles Frederick, Jordan, N. Y.; University of Michigan Homeopathic Medical School, Ann Arbor, 1904; served as coroner and health officer in Broome County; died Sept. 22, aged 74, of cerebral hemorrhage and arteriosclerosis.

Turrell, Guy Hanford, Smithtown, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1896, an associate member of the American Medical Association; fellow of the American College of Physicians; specialist certified by the American Board of Internal Medicine; president of the Smithtown Library; on the staffs of the Southside Hospital in Bay Shore and the Central Islip (N. Y.) State Hospital; died in the Ross Sanitarium, Brentwood, Oct. 7, aged 84, of cerebral hemorrhage.

Uphouse, Albert Milton, Stoystown, Pa.; Eclectic Medical Institute, Cincinnati, 1909; formerly county commissioner and coroner; for many years a member and president of the school board, on the staff of the Somerset (Pa.) Community Hospital, died in the Windber (Pa.) Hospital Sept. 20, aged 79, of cardiac decompensation.

Wells, Charles Obed ⊕ Hillsboro, Ore.; University of Oregon Medical School, Portland, 1943; died near Joseph Oct. 6, aged 54, of coronary occlusion.

Wilcox, John Constantine, Mulvane, Kan.; University of Louisville Medical Department, Louisville, Ky., 1907; died Sept. 25, aged 76.

Young, James Watson ⊕ Beverly Hills, Calif.; State University of Iowa College of Medicine, Iowa City, 1926; member of the American Academy of General Practice; served on the staff of the California Hospital in Los Angeles, where he died Oct. 15, aged 55, of rheumatic heart disease-with mitral stenosis.

Zimmering, Paul, New York City; University of Bristol Faculty of Medicine, Bristol, England, 1937; member of the American Psychiatric Association and the Medical Society of the State of New York; specialist certified by the American Board of Psychiatry and Neurology; veteran of World War II; senior psychiatrist of the male adolescent ward of Bellevue Hospital; died in the Mount Sinai Hospital Oct. 16, aged 47.

FOREIGN LETTERS

AUSTRIA

Treatment of Thrombosis.—At the meeting of the Vienna Society of Physicians on Oct. 19, Gottlob and Zinner stated that large doses of streptokinase given in the attempt to dissolve a thrombus may cause toxic reactions. Doses about 1/100 the size of those usually given are sufficient, if the enzyme is applied as a continuous infusion topically into veins peripheral to the thrombosed area. Symmetrical thromboses in the femoral veins were produced in cats. One side was infused with streptokinase and the other with Ringer's solution. The thrombus was dissolved only on that side where an infusion of 80 units of the enzyme per kilogram of body weight per hour was given. The thrombosis recurred after the treatment was discontinued or after the sides receiving the infusions were reversed. The speakers concluded that thrombolysis is limited to the veins of the treated side and that further therapy with anticoagulants is necessary after the infusions are discontinued. Excellent results were obtained in nine patients with superficial or deep thrombosis with a dosage of 1.5 to 15 units per kilogram of body weight per hour. Improvement was observed within six hours after treatment was started. Mild pyrogenic reactions were observed and were attributed to the toxic effects of the streptokinase-streptodornase infusion rather than to the fibrinolysis.

BRAZIL

Stenosis of the Stomach.—Dr. Mario Fanganiello and co-workers in *Revista paulista de medicina* (49:93, 1956) reported a series of 24 patients with stenosis of the stomach caused by the swallowing of caustic substances. In 20 patients the swallowed substance was caustic soda used for house cleaning purposes; in 2, hydrochloric acid; and in 2, more complex caustic compounds. Of the 20 lesions caused by caustic soda, the stenosis was in the pylorus in 6; in the antrum in 6; in both pylorus and antrum in 2; in the gastric fundus in 2; in the pylorus, antrum, and gastric fundus in 3; and in the antrum and gastric fundus in one. In all of these there was also stenosis of the esophagus. In the 11 patients with pyloric stenosis the lesion was manifest after a minimal lapse of 19 days and a maximal lapse of 31 months. The pyloric stenosis caused a rapid and marked dehydration and electrolytic imbalance necessitating a prompt correction. Its diagnosis is not difficult, except when the symptoms are masked by those of a stenosis of the esophagus. The diagnosis was confirmed by x-ray. The roentgenogram may show the stomach greatly diminished in volume or, when there is a prolonged stasis, somewhat enlarged, the first manifestation being the commoner. Peristalsis was always diminished. The mucosal pattern was greatly altered; in certain areas no rugae could be seen, and in others there was a thickening and edema of the mucosal folds, with a variable degree of infiltration-causing strictures. Some areas that were not destroyed showed proliferations accompanying the reparative process that appeared as small polyps carpeting the antral mucosa. Gastric neoplasms had to be ruled out. In patients in whom the pyloric obstruction appears a few years after swallowing the caustic substance, the patient may not relate his symptoms to the injury and may even forget to speak of it. Treatment consists of segmental or partial resection of the stomach.

Endoscopy in Cancer of the Esophagus.—Dr. J. A. Botelho of São Paulo at a meeting of the Associação Paulista de Medicina reported a series of 192 patients with tumors of the esophagus found in 7,100 admissions to the surgical service of the São Paulo State University Hospital. Of these tumors, 19 were in the upper third of the esophagus, 48 in the middle third, and 90 in the lower third; in 35 patients the location was not recorded. The diagnosis was made by esophagoscopy and biopsy. The speaker agreed with Vinson's statement that any firm obstacle at the level of the cardia should be considered as cancer. Dr. Botelho's experience shows that the tumors of the cardia are sometimes undiscovered even after several x-ray examinations. Esophagoscopy may not visualize the tumor, but a permanent obstacle at the level of the cardia should cause the endoscopist to suspect cancer. A possible accident in performing a biopsy of the esophagus is perforation. Anatomic peculiarities make perforation more likely in the first and last portion of the esophagus than in the middle section. In 192 biopsies performed by the author perforation occurred only once. No more tissue than is strictly necessary should be taken. The speaker never tries to go beyond the tumor with the esophagoscope or with catheters to estimate the extent of the growth, since the x-ray examination gives better information in this respect. If perforation of the esophagus is suspected, the ambulatory patient is advised to come back to the clinic without delay if there is fever or persistent pain. With the use of antibiotics the prognosis in such patients is greatly improved.

Tropical Eosinophilia.—The relationship between climate and asthma has long been recognized. Climatic factors influence asthmatic patients by different mechanisms and to a varying degree. Its importance in the determination or the aggravation of some cases is so great that such cases are commonly designated as climatic asthma. The term "tropical eosinophilia" was first used by Weingarten, in 1943, when he reported 81 cases occurring in India. For several years cases have been reported in the northeastern tropical section of Brazil. Dr. A. Coutinho in *O Hospital* (50:575, 1956) reports a series of 80 patients in Recife with this condition. Of these patients, 11 were children varying in age from infants to 9 years, 9 were 10 to 19 years of age, 12 were 20 to 29, 19 were 30 to 39, 16 were 40 to 49, 10 were 50 to 59, 2 were 60 to 69, and one was between 70 and 79. In 8 patients the duration of the symptoms was less than one month; in 45, 1 to 12 months; in 23, 1 to 5 years; and in 4, more than 5 years. Dr. Coutinho did not find evidence of any allergic cause. He describes tropical eosinophilia as a chronic benign process with cyclic nocturnal paroxysms of nonproductive persistent coughing with variable amounts of wheezing and expiratory dyspnea, sometimes preceded or accompanied by loss of weight, fatigue, fever, anorexia, thoracic pains, and upper respiratory symptoms. A diffuse mottling or an accentuation of bronchovascular striations and a hilar enlargement were the usual roentgenographic manifestations. The essential feature of the disease was an intense eosinophilic leukocytosis. Other common features were eosinophilic hyperplasia of bone marrow, an increased sedimentation rate, and negative tests for syphilis or any parasitic disease. In Recife the mean maximum temperature is 83.5 F, the mean minimum temperature is 73.9 F, and the total annual rainfall is 60.5 in.

FRANCE

Novobiocin.—R. Martin and co-workers (*Presse méd.* 64:1597, 1956) say that novobiocin, a new antibiotic, possesses an outstanding antimicrococcic action. The micrococci easily acquire, both in vitro and in vivo, resistance to the drug, but this resistance does not induce any cross resistance to other antibiotics. The bacteriostatic activity of novobiocin is impeded by alkalinity or by the presence of serum. The antibiotic becomes reversibly attached to the albumin fraction of the serum, but the bactericidal potency of the free portion remains intact. Novobiocin showed a bactericidal potency intermediate between that of penicillin and that of erythromycin in vitro against strains of micrococci. This potency was compared in vivo, by means of a quantitative test, with that of penicillin, erythromycin, and chloramphenicol and gave results similar to those obtained with penicillin. There was a bactericidal synergy between novobiocin and penicillin and between novobiocin and streptomycin, but when the new drug was given with antibiotics of the erythro-

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The items in these letters are contributed by regular correspondents in the various foreign countries.

mycin group, it provided only an additive and bacteriostatic effect. The authors reported a patient with severe micrococcic endocarditis in whom the use of a combination of penicillin and novobiocin was much more effective than had been the previous use of penicillin alone.

Icterus Caused by Inhibition of the Biliary Secretion.—I. Pavel (*Presse méd.* 64:1600, 1956) states that some cases of icterus considered to originate from hepatitis are due to functional inhibition of the biliary secretion. Of the patients he personally observed, he cites the condition of one as particularly illustrative. The icterus was shown to be prolonged, with no tendency toward remission, and accompanied by intractable pruritus in a 25-year-old man. On operation, no biliary obstruction was found and the biliary ducts were not dilated. When cholecystostomy was performed, the dark bile started flowing as early as the first hours after the operation, the pruritus disappeared, and the feces resumed their normal color. Such an icterus could not have been caused by hepatitis, because the bile flow reappeared in much less time than would be necessary for the healing of an anatomic lesion. Nor is it possible to attribute the icterus to an intrahepatic obstruction (biliary thrombus, external pressure on the canals of Hering, or increased permeability to the pigments in the latter) in view of the prompt return of the biliary secretion. The only explanation is functional inhibition of the biliary secretion.

Frenquel in Psychiatric Therapy.—H. Collomb and co-workers (*Presse méd.* 64:1602, 1956) treated 30 patients with Frenquel. They made the following conclusions: 1. To the first indications for its use (delirious and hallucinatory states) one should add the depressive state. 2. Its action proves spectacular in only a few patients, and it is difficult to predict which patients will benefit. 3. It is nontoxic, and further observation is necessary for defining more accurately its indications for use and its value as an adjuvant to other treatments.

Combined Anti-Inflammatory and Antituberculous Chemotherapy.—Pestel and Ravina (*Presse méd.* 64:1615, 1956) recommend combined therapy with phenylbutazone and isoniazid for all forms of tuberculosis where the inflammatory character of the lesions seems to predominate. They call attention to the fact that this mode of treatment not only is of value in such cases but also has proved effective in patients with pulmonary infiltrates, tuberculomas, progressive exacerbations, ulcerocavitary tuberculosis resistant to the usual therapeutics, and osseous or articular localizations of the disease. In the authors' series of 32 patients the results proved as good as those with the hormonal therapy, without any of the untoward side-effects imputed to the latter, such as dissemination or lighting up of old foci of infection. The combination therapy was well tolerated, and the treatment shortened the febrile course of the disease.

Chemotherapy of Psychoses.—Puech and Robin (*Semaine hôp. Paris* 32:3252, 1956) studied the results obtained with the use of chlorpromazine therapy and with "sleep cure" in a series of 80 women with various psychoses. Chlorpromazine was given intramuscularly for 10 days in doses of 75 to 125 mg. daily, then by mouth in slowly decreasing doses of 200 to 100 mg. daily. Sleep was not sought in those treated with this drug. The sleep cure was conducted in quiet, darkened rooms. Sleep was maintained by the administration of narcoleptic drugs and barbiturates. The daily duration of the sleep was 14 to 15 hours. The effects were studied according to the nature of the syndrome, the duration of the disease, the age of the patient, and the causative factors. Both therapy with chlorpromazine and the sleep cure proved effective in the course of polymorphic delirious exacerbations and acute delirious states. Chlorpromazine should be reserved for the forms of psychosis accompanied by agitation. In depressed states, therapy with chlorpromazine and the sleep cure were almost equally effective. Untoward effects were rare.

Vital Statistics.—In 1955 there were 313,000 marriages, 802,000 births, and 523,000 deaths, compared with 314,000 marriages, 807,000 births, and 515,000 deaths in 1954. In 1955 the death rate for infants under 1 year of age was 34.2 per thousand births compared with 36.6 in 1954.

Premature Cesarean Section.—In the March issue of *Gynécologie et obstétrique* A. Rossier and co-workers reported a series of 123 cesarean sections performed before term because of eclampsia or placenta previa. The infant mortality was 28%. In 53% of the series, the infants had to be resuscitated. The mortality rate was 66% for those premature infants whose birth weight was under 2 lb. (1,000 gm.). Close collaboration between obstetrician and pediatrician improves the infant's chances of survival.

Life of Erythrocytes in Hereditary Spherocytosis.—In the *Revue d'hématologie* (no. 2, 1956) A. Strumpf reports on the transfusion of spherocytes (1) to normal subjects whose spleen has been removed, (2) to subjects suffering from hereditary spherocytosis whose spleen has not been removed, and (3) to subjects suffering from spherocytosis whose spleen has been removed. In normal subjects whose spleen has not been removed, the life of the erythrocytes is 10 to 15 days; it reaches 100 days in normal subjects and those suffering from spherocytosis after splenectomy, but in patients with spherocytosis whose spleen has not been removed, erythrocytes survive only about 3 days. The author concludes that hereditary spherocytosis is caused by an abnormality of erythrocytes. Splenectomy relieves all the symptoms of the disease except spherocytosis.

Treatment of Tuberculosis with Nylon Nets.—In *Lyon chirurgical* for January, 1956, D. Juzbasic reports a series of 18 patients in whom the pulmonary lobe affected with tuberculosis is enveloped in a nylon net. The operation is simple. After the lobe is freed from any adhesions, it is wrapped in a net tightened around the hilus with a string. The wrapping is thus hermetic. Experiments on animals showed that the lobe is thus made void of air and collapses. After the operation, tubercle bacilli in the sputum disappear, the patients' health improves, and, four months after the operation, they may resume their occupations No complications were observed in these patients.

The Menopausal Syndrome.—In *La semaine des hôpitaux de Paris* for Aug. 26 (page 2777) Mrs. L. W. Halle, who noted that there has been an increase in the intensity and duration of menopausal disorders in recent years, presents the results of a survey of 2,000 native African women. In general, no subjective menopausal disorders were observed in women who had had no contact with Europeans, and an increase in the incidence of these disorders proportionate to the extent of the contact was seen in those who had had such contact. The author concludes that psychic as well as hormonal factors play an important role in causing menopausal disorders.

Endocarditis due to Vibrio Fetus.—Human infection with Vibrio fetus is relatively rare. L. Auquier and co-workers have reported a case in a 44-year-old man who complained of a severe headache and showed signs of septicemia. The organisms were identified with difficulty in a blood culture. The bacillus is gram-negative, thin, and actively motile. On the 10th day of the patient's hospitalization, a holosystolic souffle was noted. The authors believed the infection was caused by eating contaminated horse meat.

INDIA

Combined Primaquine Treatment of Malaria.—R. N. Chaudhari and co-workers (*Bulletin Calcutta School of Tropical Medicine*, July, 1956) report a series of 48 patients showing a fair number of asexual parasites in the blood. Five patients were given primaquine phosphate combined with chloroquine phosphate; 18 were given primaquine and amodiaquine hydrochloride; and 25 were given primaquine and quinine sulfate, all in single doses for three days. Included in the series were 14 patients with falciparum malaria, 32 with vivax malaria, one with a mixed infection, and one with malariae malaria. In the 18 patients treated with primaquine and amodiaquine, the fever subsided, with disappearance of asexual parasites, in 16 of them within two days and in 2 of them within three days Sexual parasites disappeared in 12 patients within two days and in 4 others within three to five days. The other two patients had no gametocytes in their blood. In the five patients treated with chloroquine and primaquine, the fever subsided, with disappearance of asexual parasites, within two days, and the sexual parasites disappeared in four of them within two days and in the other one within three days. In the group receiving quinine and primaquine the fever subsided, with disappearance of asexual parasites, in 21 in two days and in the other 4 in three days. Of the 20 patients who had gametocytes in their blood, these forms disappeared from 15 in 2 days, from 4 in 3 to 5 days, and from the other one in 10 days after completion of the treatment. No toxic reactions were observed.

Rhabdomyosarcoma of Spermatic Cord.—Rhabdomyosarcomas arising from the spermatic cord are very rare. D. B. Reddy and co-workers (*Journal of the Indian Medical Profession*, Oct., 1956) observed such a tumor in a 30-year-old man, who, when first seen, complained of a swelling of the right side of the scrotum of 12 years' duration and pain and a tumor in the abdomen of about three months' duration. The right testis could be felt separate from the scrotal tumor. A right orchiectomy was performed. The nodular tumor was 4 in. in diameter and large vessels were seen on its surface. Cut section showed it to be orange in color, to be soft in consistency, and to have areas of necrosis and hemorrhage. It was well circumscribed. The testes and epididymis could be identified, the tumor having its origin in extratesticular tissue. Microscopic examination revealed polymorphic areas consisting of cells of various shapes and sizes. Some were round with a central nucleus; others were ribbon-shaped showing cross striations. This established the diagnosis of rhabdomyosarcoma of the spermatic cord.

Malignant Melanoma in Indians.—M. V. Sirsat (*Indian J. M. Sc.* 10:629, 1956) reported a series of 60 cases of malignant melanoma. In every case the diagnosis was established by histological examination. Forty-five patients were in the age group 31 to 60; only one was prepuberal. In the series, 42 were male and 18 female. The tumor had arisen from the skin in 31, the commonest site being the sole of the foot. Cutaneous carcinomas other than melanomas are rarely found on the plantar aspect of the foot. A history of preexisting nevi was present in 36 to 80% of the patients. In 24, the tumor arose primarily in the mucosa of the mouth, nose, esophagus, anorectal region, or vagina. In two patients the primary site was unknown, and in one of these a metastatic tumor was found in the breast.

Carcinoma of the Breast.—Reddy and Reddy (*Indian J. M. Sc.* 10:642, 1956) state that one explanation for metastasis in malignant growths is that a diminished content of calcium in the malignant cells lowers their adhesiveness. The authors estimated the calcium content of malignant cells in primary carcinomas of the breast, their metastases, and normal breast tissue and found the calcium content of the cells in the primary and secondary tumors definitely lower than that of normal tissue. This was especially true of the metastases. Changes in the stroma may also be responsible for the dissemination of malignant growth. These changes were also studied in the same specimens by staining with toluidine blue and aminosalicylic acid. In nearly 40% of the cases studied, for example, as in the case of benign breast tumors, there was metachromasia that could not be removed by digestion with hyaluronidase. This could be due to some change in the ground substance allowing the malignant cells to infiltrate through.

Treatment of Gonorrhea with Chloramphenicol.—S. N. Ranade and co-workers (*J. Indian M. A.* 27:242, 1956) gave intramuscular injections of chloramphenicol to 22 patients with chronic gonococcic urethritis in whom other antibiotics had failed to effect a cure. Thirteen patients were given a total dosage of 3 gm. and nine a total dosage of 1 gm. in three divided doses on alternate days. The results were evaluated on the basis of urethral smears, culture of urethral discharges, smear examinations after prostatic massage, culture of prostatic discharges, and urine examination. Criteria for cure were symptomatic improvement, cessation of urethral discharge, absence of gonococci in the smear and culture of the urethral and prostatic discharges, presence of less than three pus cells in prostatic smears, and normal urine sediments. With the 1-gm. dosage schedule, the failure rate was nearly 3.5 times as great as that with the 3-gm. dosage schedule. The apparent cure rate on the 3-gm. dosage schedule was 85%.

Cytology of the Oral Cavity.—Peters and Rijsinghani (*J. Indian M. A.* 27:231, 1956) report the results of smears from the oral cavity of 595 patients with different diseases of the mouth. Smears taken from an area that harbors a cancer are usually rich in cells. In this group, 194 patients had oral carcinoma. The diagnosis was verified histologically unless it was far advanced. Biopsy specimens were obtained from 185 patients of whom 162 showed cancer on histological examination. Smears were taken from all patients. One hundred fifty-four showed malignant cells; 8 failed to show malignant cells, although a carcinoma was present; and 32 showed cells probably but not positively identified as carcinomatous. Of those patients with diseases other than carcinoma, 15 had leukoplakia, 19 had submucous fibrosis, 2 had rhinoscleroma, and the rest had such disorders as infections, ulcers, and vitamin deficiencies. In two patients, cancer was first discovered by smear, the lesions having been considered ulcerative stomatitis and hypertrophy of the tonsil respectively. A biopsy specimen in these cases revealed carcinoma. Cells desquamated by oral cancer are sufficiently characteristic to be recognized in the smear.

Employees State Insurance Plan.—The government has decided to extend the medical care under the Employees State Insurance Scheme to families of insured persons. The cooperation of the state governments is being sought to carry out the decision as early as possible. Another 3 million persons are likely to benefit when the medical care is extended to the family. The plan now covers more than 1 million employees. It will ultimately cover more than 9 million persons, including families, when extended to all of India. Under the act, insured persons are already paying the full contribution of about 2.5% of their wages, while employers are paying less. Though under the act the employers' contribution up to 5% of the total payroll can be exacted, employers have been required to pay only 1.75%. With the proposed extension of the medical care to the families of the insured employees, the rates of contribution from employers will be increased to 2.5%.

Less Familiar Forms of Leprosy.—H. W. Wade in the April issue of *Leprosy in India* states that the clinical findings in leprosy may vary in different countries or under different circumstances in the same country. Classification has become complex and is becoming more so as new forms are identified. The primary basis of classification should be clinical. The "intermediate" form is characterized by simple flat macular lesions that are early as regards development and uncertain as regards future evolution. Some will become tuberculoid, some lepromatous, and some will persist as simple macular lesions. The minor and major varieties of the tuberculoid type are relatively quiescent. Two kinds of reactions in this form are distinguished: (1) tuberculoid reactivation, which is primarily an acute activation of preexisting tuberculoid lesions, and (2) reactional tuberculoid leprosy, an abruptly developing condition. The recently recognized borderline form develops in patients with the tuberculoid form as a result of repeated or severe reactions that overcome the patient's resistance. It is often diagnosed as lepromatous because of its bacteriological positivity and lepromin negativity, but it has certain distinctive features. The condition of many patients is difficult to classify because it shows intermediate characteristics. The principal difficulty is the distinction between borderline and lepromatous cases.

Serum Iron in Visceral Leishmaniasis.—C. R. Das Gupta and co-workers (*Bulletin Calcutta School of Tropical Medicine*, July, 1956) state that anemia of a varying degree is seen in visceral leishmaniasis. The use of hematinics alone, without specific treatment, rarely, if ever, improves the blood picture. Other factors in the causation of this anemia are hypersplenism, hemolysis, and associated nutritional deficiencies of iron or antimegaloblastic factors. Other authors have shown that the serum iron and iron binding capacity of the serum are low in chronic infections. The present study was undertaken to see whether the anemia of leishmaniasis conforms to the pattern seen in chronic infection. Studies of the serum iron, iron binding capacity, and iron absorption of 29 patients with this disease were made before and after the specific treatment was started. In untreated patients these values were low as compared with those in patients with other chronic infections. There was, however, no significant correlation between the degree of anemia and the degree of depression in the values. After specific treatment, the iron binding capacity and absorption values improved, but in many the serum iron remained low. These findings indicate that, in addition to hematological values, the serum iron level can serve as an additional index of improvement. The results show that chronic infection plays a significant part in the causation of anemia in leishmaniasis.

Cutaneous Nocardiasis.—Chakraborty and Banerjee (*Bulletin Calcutta School of Tropical Medicine*, July, 1956) observed six patients with cutaneous actinomycosis in four of whom the organism was isolated and identified as belonging to the genus Nocardia. Two patients treated with sulfonamides, various antibiotics, potassium iodide, and x-ray did not respond and died of the disease. The third showed 25% improvement when put on therapy with isoniazid and aminosalicylic acid. The fourth, who had had a swelling of the left ankle with multiple sinuses for about six years, appeared to have improved clinically after five and a half months of the same treatment, but he still complained of occasional pain in the leg and restriction of movement of the involved ankle.

Synthetic Drugs for Cholera.—Lahiri and Guha (*J. Indian M. A.* 27:161, 1956) reported that earlier investigation with a crude extract named thiodiamine, obtained from the decomposition products of the barks of Crataeva roxburghii, showed good antibacterial action against Vibrio comma. Elucidation of its structural formula prompted the investigation of some related compounds, generally of phenyl and diphenyl linkages, for antibacterial properties. Four of them (orthothiocarbamidophenol, 4'-4'-dihydroxythiocarbamidophenol, ortho-aminophenol, and para-aminophenol) were found to have marked antibacterial effects against V. comma in vitro. They also showed, in varying degrees, antibacterial actions against Streptococcus hemolyticus, Micrococcus pyogenes var. aureus, Shigella shigae, and Salmonella typhosa. They had no action against Escherichia coli. They were also found to have very low toxic effects when orally administered to rabbits for a short time. On clinical trial in the treatment of cholera, their effects on death rates were inconclusive. In severe infection the antibacterial effect of para-aminophenol on stool cultures taken every four hours was found to be practically equal to that of sulfaguanidine or oxytetracycline. The effect of ortho-aminophenol appeared to be a little less. These compounds, especially the aminophenols, were not recommended for wider use without further trial.

Treatment of Malaria.—M. N. Jinda (*J. Indian M. A.* 22:204, 1956) states that an earlier experimental study on the toxicity of quinine-calcium glucono-galacto-gluconate (QCGGG) on the cardiovascular system of dogs had shown that this drug is much safer when administered parenterally as compared with quinine. He has now given a 10% solution of QCGGG intravenously to 40 patients with proved malaria. The dosage was calculated according to the age of the patient. Blood smears were checked on the fourth day and subsequently every week for four weeks. Clinical cure was obtained in 30 of these patients. The drug was found effective against Plasmodium vivax and Plasmodium falciparum but was ineffective against their gametocytes. It is not recommended for the routine treatment of malaria.

Hyperplastic Intestinal Tuberculosis.—K. L. Wig and co-workers (*Indian Journal of Tuberculosis*, September, 1956) state that an earlier investigation revealed many of the chronic granulomatous lesions of the ileocecal region to be tuberculous in origin. Although these lesions may not show the typical histopathological appearance of tuberculosis and no organisms could be isolated, the findings may change, with or without specific antituberculosis treatment, in favorable cases with progress of the disease. The authors, therefore, obtained, in a series of 42 patients, roentgenograms of the chest and gastrointestinal tract, cultures of sputum and gastric washings for acid-fast bacilli, and bacteriological and histopathological examination of the mesenteric nodes and resected loops of the small and large intestine. Clinically, most of the patients complained of a dull abdominal aching pain with acute exacerbations. Symptoms, signs, and radiologic examination pointed to a diagnosis of chronic intestinal obstruction. In group 1, consisting of 14 patients, the diagnosis was established by the isolation of Mycobacterium tuberculosis and by histopathological examination. In group 2 (14 patients) typical histopathological findings were observed but no organisms were isolated. In group 3 (14 patients) neither the bacteriological nor the histopathological findings were diagnostic, but, taken in conjunction with the clinical features and the presence of small caseous areas in some patients, these lesions were considered tuberculous in origin. Typical histopathology is not always seen, and nonspecific round cells and plasma cells may be the only evidence of tuberculous inflammation, particularly of mucous membranes. Most of the patients had had prolonged antituberculosis treatment, and healing had already started in many of them.

Paper Electrophoresis.—M. K. K. Menon and co-workers (*Journal of Obstetrics and Gynaecology of India*, June, 1956) state that serum protein values of normal nonpregnant women cannot be taken as normal standards for those who are pregnant. An investigation was therefore undertaken to obtain standard figures for the serum protein values at the full term of pregnancy and to compare those values with others obtained in women whose pregnancies were complicated. The study included 8 normal nonpregnant women of the same age group, 52 women with normal pregnancies at full term, 16 with anemia complicating pregnancy, and 13 with eclampsia complicating pregnancy. Serum protein fractions were estimated by paper electrophoresis In women with normal pregnancies at term there was a statistically significant drop in the total proteins, which was mainly due to the fall in the albumins. There was a slight rise in the serum alpha$_1$, alpha$_2$, and beta globulin values. There was no change in the serum gamma globulin value at full term. In eclampsia there was a further drop in the total proteins and albumins. The alpha$_1$, alpha$_2$, and beta globulin values showed no significant change. The lowest values of gamma globulin were obtained in eclampsia, and the fall was statistically significant. In pregnancies associated with anemia and hypoproteinemia there was a significant fall in all the fractions except alpha$_1$ and gamma globulins.

Late Abortions.—H. V. Tilak studied a series of 600 patients with abortion occurring after the fourth month of pregnancy (*Journal of Obstetrics and Gynaecology of India*, September, 1956). Of these patients, 311 were found to suffer from one or more conditions that usually cause abortion. The Rh factor played little or no part in isoimmunization of the mother to cause abortion. Nephritis was also a negligible factor. Seminal defects was a major cause if the finding of abnormal sperms in 44, or 46%, of 95 seminal specimens is applied to the series as a whole Excessive torsion or twisting of the umbilical cord was found in 12% of the cases in which the products of conception were available for inspection. Excessive twisting seems to be a cause and not a result of maceration of the fetus. The frequency and variety of pathological conditions in the placenta was an outstanding finding in this inquiry. It was found in 30% of the cases in which the products of conception could be studied. A combination of some unhealthy factors before and during pregnancy seems to increase the risk of abortion. Complete general and local examination and treatment before conception of married persons who complain of long sterility or repeated abortions, stillbirths, and premature deliveries is an important step in reducing the incidence of late abortions. The inquiry points to the importance of antenatal care and treatment of mothers from the time pregnancy is first suspected, with a view to remedying as many of the devitalizing factors as possible.

Adrenal Cortical Causes of Toxemia of Pregnancy.—R. K. K. Tampan and co-workers (*Journal of Obstetrics and Gynaecology of India*, September, 1956) investigated the activity of adrenal cortex in normal nonpregnant women, normal pregnant women, and women with toxemias of pregnancy. Significant increase in the corticosteroid excretion was noted in patients with toxemia of pregnancy. This excretion returns to normal in the postpartum period when the toxemia has subsided. A close inverse proportionate relationship between the sodium-potassium excretion ratio and the formaldehydogenic steroid similar to the relationship exhibited by aldosterone was demonstrated. Severe pyridoxine deficiency was shown to cause morphologic changes in the adrenal cortex, which returns to normal after injections of pyridoxine. Other factors of the vitamin B complex cause similar changes. A deficient niacin intake was found in patients with preeclampsia and eclampsia. This defect may be the initial stimulus resulting in enlargement of the zona fasciculata of the adrenal cortex, with increased production of corticosteroids. This, in turn, by inhibiting the production of progesterone, causes premature maturation of the placenta, producing an enzyme that ultimately acts adversely on the vascular and renal systems. Vitamins, to be effective in the prevention of toxemia, should be given in the first month of pregnancy, as such supplements may fail to reduce the incidence of preeclampsia and eclampsia once the placenta is formed.

NORWAY

Testing of New Drugs.—At an Inter-Scandinavian medical conference last summer a discussion centered about the merits and ethics of double-blind testing of new remedies. Prof. O. J. Broch of the University of Bergen stated his views on the subject in the daily newspaper, *Aftenposten*, for Oct. 5. He recalled that a few years ago the world at large was tricked into believing in fantastic claims on behalf of chlorophyll, which was not tested by this method. It is ethically indefensible to give inert tablets when the drug to be tested has self-evident merits and the disease in question is serious, but the situation is somewhat different when the merits of a certain remedy are in doubt and its prolonged use is costly. As a case in point, Professor Broch referred to the treatment of angina and other manifestations of heart disease with anticoagulants. Were this treatment to be applied wholesale to such patients, the cost to the community would be enormous and the patients would have to submit to tedious years of close medical supervision. Here, then, is a field in which the judicious treatment of alternate patients should help to clarify matters. Anticoagulants have proved useful in certain diseases, but we have yet to learn exactly which they are and under what special conditions. Professor Broch concludes that we are not justified in dispensing with this test for distinguishing between potent and impotent remedies.

The Choice of Site of BCG Vaccination.—The BCG laboratory in Bergen acts as a clearing house for information on BCG vaccine. Its latest advice is to shun the thigh as a site for vaccination because of the greater risk of severe local reactions and regional adenitis after an intracutaneous injection. The outer aspect of the upper part of the arm is to be preferred, and whoever insists on vaccination of the thigh should be warned of the risk.

Smallpox Vaccination.—The new smallpox vaccination law that came into force on July 1, 1955, was framed to encourage such vaccination early in life to reduce the risk of postvaccinal encephalitis to the minimum. According to this law vaccination should be carried out before the end of the calendar year following that in which a child is born. The sponsors of this law also emphasized the importance of educational propaganda addressed to the educated as well as to other elements of the community. An investigation undertaken by Dr. K. H. Torp (The Journal, Dec. 24, 1955, page 1675) showed that the medical profession does not set as good an example in this respect as it should, but early vaccination has of late been more popular than it was, to judge by a study of the subject published in *Tidsskrift for den norske lægeforening* for Oct. 1 by Dr. T. Bjerkedal, who has scrutinized the vaccination records of school children in Oslo. Four schools, representing different social strata, were studied, and the parents were graded in four different groups according to their social standing. The lowest social group had the lowest vaccination rate, and 62% of the total of 4,608 children had already been vaccinated. About 53% of the vaccinated children had been under the age of 2 years when vaccinated. What was encouraging and indicative of the value of popular health propaganda in recent years was the rise in the relative number of early vaccinations. Thus only 33.5% of the children born in 1941 had been vaccinated under the age of 2, as compared with 63.9% of those born in 1947.

Fibrositis of the Breasts.—Dr. H. Schartum-Hansen has found that the pain and tenderness associated with chronic fibrositis of the breasts tend to disappear after only a few days' treatment with corticotropin (*Nordisk medicin*, Oct. 25). The four patients in his series ranged from 20 to 36 years of age, and the total dosage of the drug, given for five to nine days, ranged from 0.6 to 1.0 gm, the initial dose being from 100 to 200 mg. The disappearance of pain and tenderness coincided in some patients with diminution or disappearance of palpable swellings.

UNITED KINGDOM

Smoking and Cancer of the Lung.—In October, 1951, Prof. A. Bradford Hill sent to each of the 59,600 members of the medical profession in the United Kingdom a questionnaire asking information about their smoking habits; 40,701 adequate replies were received. Since then, the registrar general has given Professor Hill details of every death of a physician. With Richard Doll (*Brit. M. J.* 2:1071, 1956), Hill has now analyzed the findings for the 53-month period from November, 1951, to March, 1956. During this period there were 1,854 deaths. Of these, 1,714 occurred in men 35 years of age and above. This group forms the basis for the authors' report. Of these 1,714 deaths, 81 were due to cancer of the lung.

The analysis shows a marked and steady increase in the death rate from cancer of the lung as the amount smoked increases. Thus, the annual death rate from cancer of the lung rises from 0.07 per 1,000 in nonsmokers to 0.47 per 1,000 in smokers of 1 to 14 gm. of tobacco a day (1 gm. is approximately equal to one cigarette), to 0.86 per 1,000 in smokers of 15 to 24 gm. of tobacco a day, and to 1.66 per 1,000 in smokers of 25 gm. or more of tobacco a day. In other words, the death rate of heavy smokers was about 20 times that of the nonsmokers. The rising mortality from cancer of the lung in smokers compared with nonsmokers and in heavy smokers compared with light smokers was observed in each of four age groups: 35-54, 55-64, 65-74, and over 75. The mortality from cancer of the lung was substantially and significantly greater in cigarette smokers than in pipe smokers. The annual death rate from this cause rose from 0.95 per 1,000 in smokers of 1 to 14 cigarettes a day to 1.67 per 1,000 in smokers of 15 to 24 cigarettes a day and to 2.76 per 1,000 in smokers of 25 or more cigarettes a day. The death rate of heavy smokers was about 40 times that of nonsmokers.

Evidence is produced suggesting that giving up smoking reduces the risk of dying of cancer of the lung. The annual death rate per 1,000 in those who had given up smoking for 10 or more years was 0.35, as compared with 0.59 in those who had given it up for less than 10 years and 1.03 in those who were still smoking. In other words, the mortality from this cause among current smokers was three times as great as that among men who had given up smoking for 10 or more years and 76% greater than that in men who had given it up within the previous 10 years. Since an analysis of a random sample of questionnaires showed that there was remarkably little difference between the smoking habits of physicians residing in Greater London, in large towns, and in other districts, it is concluded that the contrasts in lung cancer mortality between smokers and nonsmokers cannot be attributed to a differential exposure to atmospheric pollution that happens to be associated with smoking habits.

Study of the deaths from cancer in sites other than the lung did not reveal, other than for one possible exception, any association between mortality and smoking. The exception was cancer of the upper respiratory and digestive tracts, from which the number of deaths was insufficient to substantiate a possible trend. In total, mortality from cancer of sites other than the lung was 2.04 per 1,000 in nonsmokers and 2.02 per 1,000 in smokers. Mortality from coronary thrombosis showed a slight but significant relationship with smoking, but the trend was distinct only in the 35-to-54-years age group. Three other causes of death showed a steady increase in mortality from nonsmokers to heavy smokers: chronic bronchitis, peptic ulcer, and pulmonary tuberculosis, but only with chronic bronchitis was the increase significant, rising from 0.12 per 1,000 in nonsmokers to 0.72 in heavy smokers.

Smoking and Pulmonary Tuberculosis.—In the same issue of the *British Medical Journal* (page 1081), C. R. Lowe reports his findings in a group of 1,200 patients with respiratory tuberculosis. Among patients in both sexes of over 30 years of age with pulmonary tuberculosis there was a highly significant small number of nonsmokers and light smokers and a very large number of moderate and heavy smokers. The persons used by the author as controls came from certain sections of the local hospital population. He found that 11.7% of the tuberculous men were nonsmokers or had smoked less than 10 cigarettes a day as compared with 21% of the controls, while 50.1% of them had smoked 20 or more cigarettes a day as compared with 43.4% of the controls. From this he concludes that smoking may be an important cause of the breakdown of healed or quiescent respiratory tuberculosis in adults and may account for much of the excessive male mortality in middle and late life. This excessive mortality rate has become a marked feature in most large industrialized countries in recent years.

Increase in Scabies.—There has been a significant increase in the number of patients with scabies, according to Dr. F. F. Hellier, in the *British Medical Journal* (2:1117, 1956). A disturbing feature is the fact that in most cases the diagnosis is unsuspected by the general practitioner. Hellier, a dermatologist, suggests that 10 years of almost complete absence of scabies has tended to make older practitioners forget the diagnosis, while the new generation has not become familiar with it.

Faulty Feet.—Dr. I. Gordon, health officer for Ilford, reports that, of 1,400 school children between the ages of 9 and 10 years, drawn from all social levels, 468 had foot defects. Hallux valgus was more common among girls, accounting for 34% of all defects, compared with about 12% for boys. More girls had curled toes, presumably due to the wearing of tight shoes. The incidence of flat feet was equal in both sexes, but the number of boys with valgus ankles was double that found in girls. None of the children complained of pain in the feet or legs.

The "Open Door" in Mental Hospitals.—In his annual report for 1955, Dr. P. K. McCowan, the superintendent of Crichton Royal, Dumfries, one of the largest and oldest mental hospitals in the United Kingdom, reports that 6 of the 10 admission wards and 27 of the 31 long-stay wards in the hospital are now open. This means that 966 of the patients are in open wards and 266 in closed wards. Many of the patients in the closed wards are on parole, which means that it is only administrative necessity that prevents an even higher proportion of the patients from being in open wards. During the year, treatment with chlorpromazine and reserpine has continued to be tried out on an extensive scale, with very satisfactory results. In this period 16 standard leukotomies were performed. The results were in accordance with the hospital's last follow-up study, which showed that 34% of the patients undergoing leukotomy had been discharged socially recovered and that most of these were gainfully employed; a further 33% were much improved, although they still required hospitalization. The best results continue to be obtained in those whose preoperative personality was largely intact and who had well-adapted personalities before their breakdown. With few exceptions the patients operated on were those with schizophrenia who failed to respond to other methods of treatment and who were otherwise destined to spend the remainder of their lives as severe mental invalids. To date, 504 leukotomies have been performed on 450 patients, of whom 37 have had a second and 4 a third operation.

Tubercle Bacilli in Pasteurized Milk.—In Great Britain two main methods of pasteurizing milk are officially recognized. In the holding method the milk has to be retained at a temperature of not less than 145 F and not more than 150 F for at least 30 minutes and must be immediately cooled to a temperature of not more than 50 F. In the high-temperature short-time (H. T. S. T.) method the milk has to be retained at a temperature of not less than 161 F for at least 15 seconds and be immediately cooled to a temperature of not more than 50 F. In the holding method the milk is kept in a closed vessel during the whole time of its exposure to the prescribed temperature. In the H. T. S. T. method it flows continuously through a tube or a series of plates, which have to be adjusted so as to insure that every particle of milk receives the necessary amount of heat. During the years 1949 to 1952 an investigation was made by 22 public health laboratories in England and Wales concerning the presence of tubercle bacilli in milk pasteurized by these two methods. In the report of the investigation (*Month. Bull. Min. Health* 15:232, 1956) it is stated that, of the milk samples treated by the holding method, 8 of 201 giving a positive phosphatase reaction produced tuberculosis on injection into guinea pigs; none of the 524 giving a negative phosphatase reaction did so. Of the milk samples treated by the H. T. S. T. method, 2 of 93 phosphatase-positive samples produced tuberculosis in guinea pigs, but there was reason to believe that these 2 were raw milk samples used in error. Of 3,507 phosphatase-negative samples, one contained tubercle bacilli that were apparently derived from a filling machine used for tuberculous raw milk and one produced minimal lesions in the guinea pig. The lesions were reported at the time as being tuberculous, but the subsequent examination showed them to be almost certainly not due to the tubercle bacillus. As only a small proportion of phosphatase-negative milk samples were injected into guinea pigs, these figures cannot be used for calculating the real incidence of tubercle bacilli in pasteurized milk, but they can be used for comparing the efficacy of the two methods. They show that 8 of 725 (1.1%) samples treated by holding and one of 3,600 (0.03%) samples treated by the H. T. S. T. method contained tubercle bacilli. Although these results are taken to indicate that the H. T. S. T. method is the more satisfactory, it is noted that samples of milk reacting positively in the phosphatase test occur sufficiently often to justify more stringent control of processing, particularly of the smaller plants, by the sanitary authorities.

Psychosomatic Disease in General Practice.—Psychosomatic disease accounts for 15 to 20% of all the illnesses seen in an average practice in Great Britain, according to John Fry (*Practitioner* 177:554, 1956). In his own suburban practice of 5,000 patients, the most common psychosomatic disorders are hypertension (6%), migraine (2.8%), duodenal ulcer (2.5%) and asthma (1.3%). Other psychosomatic conditions treated included rheumatoid arthritis, fibrositis, ulcerative colitis, hay fever and vasomotor rhinitis, thyrotoxicosis, and menstrual and skin disorders. With the exception of hypertension, the incidence of which rises with age, and of asthma, which has its maximal incidence in childhood, most of these disorders occur in patients between 30 and 60 years of age. There is much sex variation. In the case of duodenal ulcer, men outnumber women 4 to 1, whereas in the case of hypertension, migraine, rheumatoid arthritis, and thyrotoxicosis, women outnumber men 4 to 1. The sex distribution is fairly equal in asthma, fibrositis, and the psychosomatic dermatoses. It is rare for a patient to suffer from more than one of these psychosomatic disorders at any one time. The only group of disorders to which some of these patients are prone are the effective neuroses; this is particularly evident in patients with migraine and duodenal ulcer. It is also unusual in the course of these disorders to find any sudden and obvious emotional stresses resulting in a consequent psychosomatic episode. It is much more usual to find that the summation of a series of hidden stresses is responsible.

In a seven-year period 36 of the author's 305 hypertensive patients, or 12%, died. In only 62 (20%), and this included many who subsequently died, were there any complications, and in only 35 (11%) were there any subjective symptoms related to complications. Of 145 patients treated for migraine 93 (63%) were well controlled, 42 (29%) were moderately well controlled, and in 11 (8%) there was failure to improve. Medical treatment kept 75% of the patients with duodenal ulcer relatively free from symptoms and at work. In the same seven-year period, of the 67 patients with asthma 2 died, 2 were severely disabled and unable to work, 8 were moderately disabled and required more-or-less continual therapy, and the remaining 55 (82%) were all leading normal lives with only occasional and minor episodes, which required either no specific treatment or merely ephedrine by mouth or inhaler.

CORRESPONDENCE

HYPERGLYCEMIA AND GLYCOSURIA FOLLOWING CHLORPROMAZINE THERAPY

To the Editor:—On the medical service of a large neuropsychiatric hospital, the following observations have been made during the past eight months in patients receiving chlorpromazine (Thorazine): 1. Five patients developed transient hyperglycemia and glycosuria, which disappeared upon cessation of drug use. 2. In five patients with previously controlled diabetes, the disease became unstabilized (higher blood sugar levels plus glycosuria) while they were receiving this agent. The condition of these patients reverted to prior status when chlorpromazine therapy was discontinued. 3. Two patients who had normal fasting blood sugar levels and negative urinalyses before drug therapy developed overt though mild diabetes mellitus during drug use; these conditions did not revert to normal when the drug was withheld. No present correlation has been made with the age of the patient, diagnosis, duration of hospitalization, sex, or dose or duration of chlorpromazine therapy. It is realized that this apparent relationship of chlorpromazine to a diabetic state may be fortuitous; such effects have apparently not been described previously, but their importance necessitates clarification of this possibility.

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HOBBIES

To the Editor:—I am greatly interested in the Leisure Corner articles in The Journal, especially those that deal with the development of various hobbies to fill whatever minutes the busy physician can "steal" from his daily routine. I am one of those whose hobbies are collecting stamps and playing chess. I will deeply appreciate hearing from any accredited members of the American Medical Association who also collect stamps, with the end in view of corresponding and exchanging stamps with them.

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CONGENITAL DEFECTS

To the Editor:—I certainly agree with Dr. Ingalls (*J.A.M.A.* 161:1047 [July 14] 1956) that "it is high time for orderly scientific methodologies to be used in the study of . . . congenital defects," but until the results of such studies are available for evaluation one cannot judge how far the findings of experimental teratology are applicable clinically. Dr. Ingalls has obtained evidence from experiments with mice that maternal hypoxia (or some related factor) can lead to developmental defects. From this he concludes that hypoxia is a "nonspecific stress." What exactly does he mean by "stress"? He goes on to say "Stress, of course, is to be defined more broadly than hypoxic stress" since other noxious agents such as x-rays, vitamin deficiencies, cortisone (and, he might have mentioned, genes) produce similar defects. Furthermore, he states, "a constellation of adverse maternal factors . . . anemia, hypothyroidism, organic heart disease, systemic hypertension, retroflexion, and tumor of the uterus" may affect the maternal organism in such a way that it triggers off "critical stress that leaves its impress on the conceptus for life," and, elsewhere, "The evidence is overwhelming that many, if not most, anomalous children have survived a temporary intrauterine stress" (in the summary the "many, if not most," changes to "most"). To paraphrase his argument—stresses are those factors that produce congenital defects. Therefore, congenital defects are caused by stresses. This is perfectly logical but does not improve our understanding of the causes of congenital defects. In order to prove that any given factor is teratogenic in humans one must begin by demonstrating either (1) that pregnancies exposed to the factor produce defective offspring more often than otherwise comparable pregnancies not exposed to the factor or (2) that the factor occurred in the pregnancies leading to defective offspring more often than in otherwise comparable pregnancies not leading to defective offspring. The only statistical evidence Dr. Ingalls quotes was obtained by the second method and concerns the prevalence of retroflexion of the uterus in 50 mothers of Mongoloid babies (24%), as compared to that in the mothers of a control group (8%). Here the difference between the two groups is not statistically significant, even at the 5% level, and hence may well be attributable to sampling error, rather than to any causal relationship. Although there is undoubtedly some truth in what Dr. Ingalls says, we have yet to find out how much. Until we have some solidly based clinical data, collected without bias, there is no justification for applying the findings of experimental teratology to humans.

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STUDY OF SKELETONS

To the Editor:—J. Walter Wilson, M.D., in "Dividing Lines in Specialized Medical Practice" (*J. A. M. A.* 162:1025 [Nov. 10] 1956) states: "Studying bones recovered from early Stone Age strata, LeBaron found the skeletons of 18 men who had had fractured limbs, only 3 of which would be considered to have healed poorly, even by today's standards, thereby indicating that there were persons then living who had become expert at setting fractures." Although it is recognized that these statements are purely for background purposes in the development of his main topic, specialized medical practice, perhaps correction of two errors in the quotation above is worthwhile. First, LeBaron's study was concerned primarily with the neolithic rather than the paleolithic period (Palès, L.: Paléopathologie et pathologie comparative, Paris, Masson & Cie, 1930). Second, although granting that surgical skills had been developed in the neolithic period (e. g., trephining), the argument for this on the basis of position of healed fractures is not considered valid. Schultz has shown that well-healed fractures occur in significant proportions in wild anthropoids, among whom specialized medical skills are not highly developed (Schultz, A. H.: Notes on Diseases and Healed Fractures of Wild Apes and Their Bearing on Antiquity of Pathological Conditions in Man, *Bull. Hist. Med.* 7:571, 1939). This comment is submitted to clarify a statement made by Wilson in an otherwise excellent paper. It is hoped this observation will not be considered as mere academic sophistry.

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MEDICAL AUDIT OF TESTIMONY GIVEN IN COURT

To the Editor:—Each county medical society should establish a medical audit of testimony given in court. This will give every testifying physician a score. Offenders with low score in honesty, integrity, and reliability of testimony can then be summoned before the executive committee and warned. If the practice of testifying "one way or the other" flagrantly persists, that physician should be dropped from the society. If he is a diplomate of any American board or college, this would really hurt. If not, the opposing lawyer could ask "Are you a member of your county medical society?" and "Why not?" I believe there is no need to explain at whom this is directed. It should clear the air around the courts; lawyers and the public would have more respect for the physician. Perhaps The Journal could circulate this need until it jells into concrete reality.

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THE LEISURE CORNER

TIME OUT FOR CLOCKS

"Tick-tock" is a sound that masks ages of calculation; "ding-dong" is a sound that covers centuries of mechanical invention. The movement of the hands on the face of a clock, any clock, is a recording of infinity by man's measuring stick known as time. For time, says the philosopher, is a dimension. Astrophysicists now aver that the universe is in a state of constant change, reiterating the declamation of an ancient prophet, "A thousand years is but a day to God, and a day is a thousand years." We are told that if man could fly at a speed greater than light, he would be able to squat somewhere in space and see the construction of the pyramids.

Doctors who profess an interest in clocks enjoy their hobby without waiting for the coming of incredulous rates of speed and travel; indeed, they are unconcerned with machines that will measure the fourth dimension. These earth-bound, time-bound hobbyists enjoy clocks not only for their ability to keep accurate time but also for their intrinsic worth as decorative objects for the home.

An appreciation of old clocks usually comes naturally. A clock that holds considerable appeal for most collectors is the English clock, which has a twofold claim to recognition. First of all, if it be a fine old English clock, it will prove a reliable, accurate timekeeper. Secondly, clocks from certain periods are representative of styles of decoration now equaled but not surpassed by copyists. The English clock is actually a monument to a type of superb craftsmanship now almost extinct.

To set out to buy an old clock is for the beginner an experience akin to starting out to buy a horse. In the latter instance, a horse's teeth may be filed down and the hoofs pared to simulate equine youth. In an old clock, however, it is possible to add touches that will serve as a pretense for antiquity—a pair of old hands here, an antiquated-looking dial there, and an enshrining case of no particular period at all. Taken together, this could seem time's classic imprint of age. Then one might be induced to quote the Merchant of Venice, "I never knew so young a body with so old a head."

When one is contemplating the purchase of a clock, the case, the dial, and the hands should be studied very carefully. It is important to detect errors made by clumsy repairers and unskilled restorers who, often as not, have destroyed fine work. Moreover, there is the movement to be considered, the mechanism that makes a clock a truly worthwhile clock. These features are often overlooked by the average snapper-upper of old clocks or, when they are seen, not understood.

A clock is an ornament in a well-appointed home, whether it is located in the hallway, in the living room, or elsewhere. The contemporary collector wants a clock not so much because it is of ancient vintage but because he correctly assumes there are certain qualities represented in an old clock maker's art that are not to be found in later periods. A wise collector will not place himself in the hands of a dealer who has sold a thousand clocks, but in the hands of a practical clock maker, a trained artisan with a knowledge of old movements and one to whom clocks are more than inanimate objects. For him a clock is something with a soul.

Then there is the brass lantern clock, which usually appeals to the artist. In the famous painting "The Doctor," by Samuel Luke Fildes, there is a brass clock that adds a sense of immediacy to the emotional impact of the scene. The Old Masters frequently used brass clocks and candelabra to grace the paintings of interiors in the Low Countries. The reason for the name of the lantern clock may puzzle the contemporary collector. Its shape follows that of the lantern of the period in which the form was introduced, and it was made to hang on a wall. Form and usage determined its name, although, because it has spiked hooks to hang on, it is also known as a bracket clock.

The grandfather clock has no equal within its limits. It runs for eight days, and its construction is so lacking in mechanical guile that, when a repair job is required, a specialist need not be called. The grandfather clock has survived for two centuries or more as a standard English clock. The popular, endearing name suggests a certain amount of fascination for many people; indeed, it has been called the heritage of the poor, since it passes down from one generation to another. It is often cherished as an article of furniture and sometimes endowed with a value far greater than its actual worth.

The Shepherd or del Pastor, as it is known in Madrid, is one of the most celebrated clocks in the world. It has an automaton and an astronomical mechanism and apparently is the only clock known to possess such unusual functions. This clock indicates hours, minutes, and seconds, strikes hours, and repeats the hours, quarter-hours, and half-hours. The center of the dial presents the equation of time; a yearly calendar of the day, which corresponds to the length of each month; a calendar of the moon; signs of the Zodiac, which appear at the same time as the sun; the four seasons of the year; and an artificial solar dial, which indicates the hours by means of a visible shadow. Above the integrated center is a celestial vault, in which stars appear and disappear at the same time as seen in the heavens. The sun and the moon follow their respective courses according to the system of Ptolemy. This amazing clock displays the sun declining with the seasons. The moon in its different phases, despite its various positions, always appears illuminated on the side opposite the sun. When the weather turns rainy, the clock shows a cloudy sky covered with artificial clouds; these disappear the moment the sky clears.

Moreover, when the hour strikes, one hears a carillon of six airs, part of which are played as an echo. Stationed on a balcony is a lady, who is seated holding a book in her hand and beating time to the air that is played. She moves the book close to her eyes, takes a pinch of snuff several times, and bows gracefully whenever the glass covering of the clock is opened. After the carillon, a canary whistles six airs while moving its beak and body. The canary is perched on the fist of a Cupid, who by his gestures appears to be admiring the bird. Just as soon as this performance is terminated, a life-like shepherd, demonstrating tongue control and cadences, plays several airs on his flute. While this is going on, two Cupids balance themselves to the tune of the air being played. Although their movements are rotary, their stance remains upright. As a finishing touch to their performance, one of the Cupids falls over and, turning to the spectators, gestures to his friend as though to ridicule his own unsteadiness. All parts of the clock function separately without difficulty. These are the accomplishments of this famous clock that once won the admiration of the Spanish court.

The universally known cuckoo clock was first made by Anton Ketterer, of Schönwald in the Black Forest of Germany, in 1730. The charm exhibited by the cuckoo clock has captured the heart of many clock fanciers. Children especially love to watch the cuckoo bird call out the hour and the half-hour. Pediatricians have found that the younger generation will respond to the call of the cuckoo more readily than to "who's next please?" Sizes of the cuckoo clock vary, and cost depends on the carvings of the wood, the intricacies of the design, and, of course, the quality of the movement.

During the past few years the 400-day clock has become a favorite in many American homes. It is also known as an anniversary clock. During an annual celebration, held in Germany where these clocks are made, every owner winds his clock on the same day and follows this event up with social merriment. Hence, the name anniversary clock. Every month, hundreds of anniversary clocks are sent to this country as gifts. Today, it is estimated that there are over 2 million old and new 400-day or anniversary clocks in the United States alone, with more being shipped in every day.

Any clock that appeals to collectors, whether it is a hall clock, chime clock, water clock, or a banjo clock, has the potential value and interest that an antique would have. Imitation is the sincerest form of flattery. A thousand replicas usually start up a demand for a particular type of clock. The hobbyist of taste says that such and such a clock is unique in its artistic appeal to him. The collector with money purchases as many "uniques" and antiques as his distended bank account will encourage.

Several centuries ago Francis Bacon wrote, "If a man be in sickness or in pain the time will seem longer without a clock or hourglass than with it." It was once rare for a doctor to visit a sick patient and find a clock missing from the bedside. The clock frequently seemed to beat the very rhythm of life into the heart of the patient. Many patients became startled when the "tick-tock" of the clock ceased. The breath of life, they imagined, was sponsored by the rhythm of the bedside clock, and so small a detail as winding a clock made them aware that they were in full possession of their faculties.

"Doctors' Legacy"

Those who were interested in the article "The Doctor Writes a Letter" (Leisure Corner, *J.A.M.A.* 162:236 [Sept. 15] 1956) can find a detailed treatment in the book "Doctors' Legacy," the author of which is Dr. Laurence Farmer. This book was published by Harper & Brothers in 1955.

LAW DEPARTMENT

MEDICOLEGAL ABSTRACTS

Medical Examiners: Can They Be Forced to Conduct an Inquest?—The medical examiner of Wayne County, Michigan, was directed by the county's prosecuting attorney to conduct an inquest in a particular case, as distinguished from an "investigation" provided in the act creating the office of medical examiner. A writ of prohibition was filed seeking to restrain the medical examiner from so doing and the case was heard in the Supreme Court of Michigan.

The question, said the court, is one of interpretation of act 181 of the Michigan laws of 1953. By Section 2 of this act the county medical examiner is obligated to make examinations upon the bodies of designated persons. By Section 5 his investigative procedures are, as the counsel for respondent say, "all spelled out." So far the act hints no duty or authority respecting the summoning of a jury and the holding of an inquisition according to time-honored practice. Section 7 provides that upon the written order of the prosecuting attorney or attorney general, or upon due filing of a petition signed by six electors of the county, the county medical examiner shall conduct an investigation according to the procedures set forth in Section 5. Section 13 then provides: "In counties having a medical examiner under the provisions of this act, the powers and duties vested by law in the office of coroner are hereby transferred to and vested in the county medical examiners and their deputies. In such counties immediately upon the taking effect of this act, the office of coroner shall be abolished, and whenever reference thereto is made in any law of this state, reference shall be deemed to be intended to be made to the medical examiners created by this act, insofar as consistent with the provisions of this act. Any hearing or other proceeding pending before any coroner shall not be abated but shall be deemed to be transferred to the medical examiner of the proper county and shall be conducted and determined by such examiner in accordance with the provisions of law."

The prosecutor contended that all of the previously known powers and duties of coroners, including the power and duty of jury inquisition and functions thereof, were transferred by this section to the county medical examiner. The respondent says that on the strength of the words "insofar as consistent with the provisions of this act" the power and duty of coroner-jury inquisition was not so transferred.

The purpose of the medical examiner act, said the Supreme Court of Michigan, was to eliminate the senescent "crowner's quest" in counties where the electorate decided by the terms of the 1953 act to accept the principle of pathological investigation in lieu of coroner-jury inquisition. We find that the legislature intended that the act extends investigative power only, as defined in sections 1 through 12, to the medical examiner of Wayne County. As was said in a New York decision, "The chief medical examiner acts without a jury, holds no inquest, renders no decision, holds no one to answer, issues no warrant of arrest. The ancient office is gone and the ancient duties have largely disappeared with it. Another method of investigating suspicious deaths has supplanted crowner's quest."

Accordingly the Supreme Court approved an order restraining the medical examiner from summoning a jury and conducting an inquest in the case in question. *Lipiec v. Zawadski and O'Brien, 77 N. W. (2d) 763 (Mich., 1956).*

Right of Unlicensed Person to Use "M.D." Degree.—The plaintiff filed a petition against the Board of Medical Examiners to enjoin it from prosecuting him for alleged statutory violations. From an adverse judgment by the district court, the plaintiff appealed to the district court of appeals, second district, division 2, California.

The plaintiff graduated from a medical school in Ohio and practiced medicine in that state for a number of years. He then moved to California and founded the Lawton School for Medical Assistants. In certain advertising material in connection with this school, the plaintiff used his name, followed by the letters "M.D." The defendant board contended that such action was a violation of Section 2142 of the California law that provides: "Any person, who uses in any sign, business card, letterhead, or in an advertisement the word 'doctor,' the letters or prefix 'Dr.,' the letters 'M.D.' or any other term or letters indicating or implying that he is a physician and surgeon, physician, surgeon or practitioner under the terms of this or any other law, or that he is entitled to practice hereunder, or under any other law, without having at the time of so doing a valid, unrevoked certificate as provided in this chapter, is guilty of a misdemeanor."

The plaintiff first contended that because he was not engaged in the practice of medicine, the section could not in reason apply to him and that the section was therefore unconstitutional as to him because it deprived him of a valuable property right, to wit, the right to the use of the letters "M.D." to indicate the area of his professional training.

Conceding, *arguendo*, that the plaintiff has a property right in the significant letters, said the court, still it must be acknowledged that such right does not take precedence over the public welfare that the section seeks to conserve. It is apparent that the legislature may well have deemed it wise that those who instruct in the science of medicine should be forced to disclose their educational backgrounds and that they should not be allowed to mislead students into thinking their instructors are licensed to practice medicine in California. If in fact the teachers have had excellent medical training, there is nothing in the law that prevents them from indicating such fact. Medical schools do not uphold equally the same high standards, nor does California maintain reciprocity in the medical field with all other states. The student and the public are entitled to know the qualifications of those who directly or indirectly affect the public welfare as does the medical profession. Neither graduation from a reputable institution nor want of sufficient education will excuse the necessity of being certified before a person may advertise his right to adorn his name with Dr. or M.D. Such letters are false insignia when a physician attempts to tell the world he is licensed when in fact he is not. Whether they actually practice here is immaterial. The intent of the legislature was to shield the public against those who for any reason have not been duly licensed. The plaintiff's offense, said the court, was in holding himself out as a physician in this state although he does not possess a valid license to do so.

The plaintiff also contended that the section could not be justified under the police power because it had no relation to the public health or safety as applied to him. A person in California who holds himself out to the public as a licensed physician and purports to teach here the science of medicine and the art of its practice to students to enable them to pass California examinations, said the court, is clearly liable under the section and the public is aggrieved by his representing himself in the manner forbidden by the statute. The legislature intended every person engaged in professional activities properly to represent himself in his true capacity by appropriate title.

Other contentions of the plaintiff were also overruled and the plaintiff's request was denied. Judgment for the defendant Board of Medical Examiners was affirmed. *Lawton v. Board of Medical Examiners, 299 P. (2d) 362 (Calif., 1956).*

ILLUSTRATED FILM REVIEWS

Illustrated reviews of current films will appear when possible as a regular feature in The Journal. *They will consist of an introduction by the author followed by a pictorial digest of actual frame enlargements selected as key points of the film. This type of review should enable clear visualization of the author's treatment or technique.*

The first few illustrated reviews will be based on films for which a regular review has already been published; however, it is planned in the future to publish both the illustrated and printed review of current films in the same issue.

Ralph P. Creer, *Director Motion Pictures and Medical Television, Council on Scientific Assembly*

SURGICAL TREATMENT OF DISSECTING ANEURYSM

Michael E. De Bakey, M.D., Denton A. Cooley, M.D.
and
Oscar Creech Jr., M.D., Houston, Texas

Dissecting aneurysm of the aorta is associated with a grave prognosis, but recently a method has been developed that seems to offer an effective surgical approach to the problem. The underlying predominant lesion is degeneration of the elements of the media. The dissection commonly begins as a transverse tear in the intima and media in the ascending aorta or descending limb of the aortic arch near the origin of the left subclavian artery. Separation of the intramural layers of the aorta by the forceful stream of blood produces dissection involving all or a portion of the circumference of the aorta. Surgical treatment is directed toward correction of the dissecting process by removal and repair or interruption of its progress by creation of conditions compatible with function and eventual repair. One of two methods may be used, the first when the dissection originates in the ascending aorta and the second when it begins near the origin of the left subclavian artery. This method has been successful in 14 of 18 cases, with an operative mortality of 22%. Follow-up over two years indicates highly gratifying results. (This film was reviewed in The Journal, Nov. 10, page 1078.)

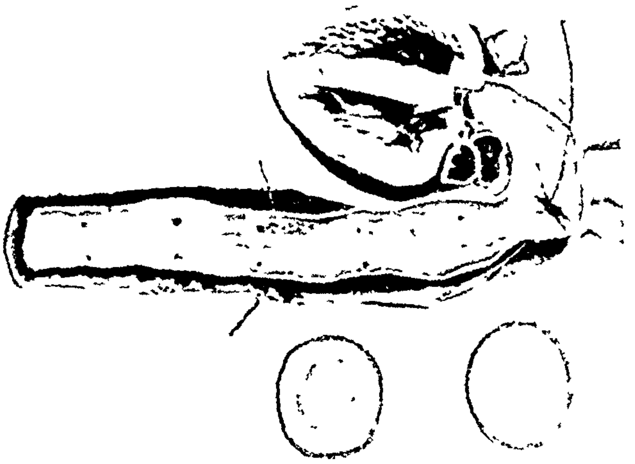

Fig. 1.—Drawing showing pathological features of dissecting aneurysm

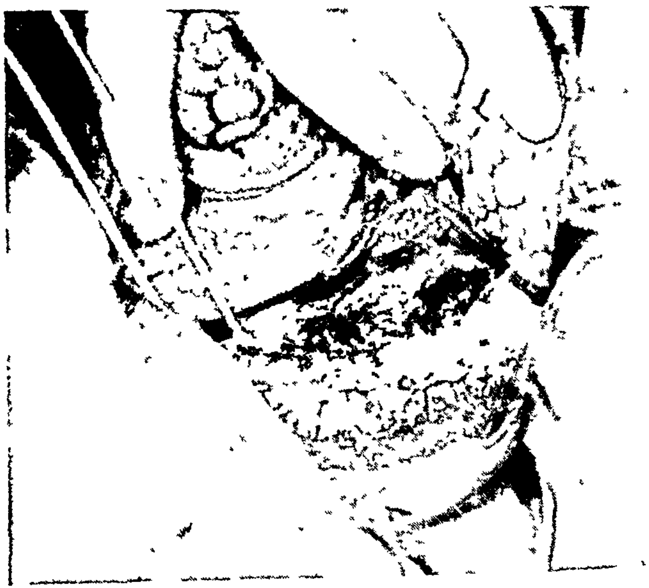

Fig. 3.—First step in operation, exposing descending thoracic aorta through left posterior lateral thoracotomy. Dilated aorta is freed from its bed and encircled above and below with umbilical tape

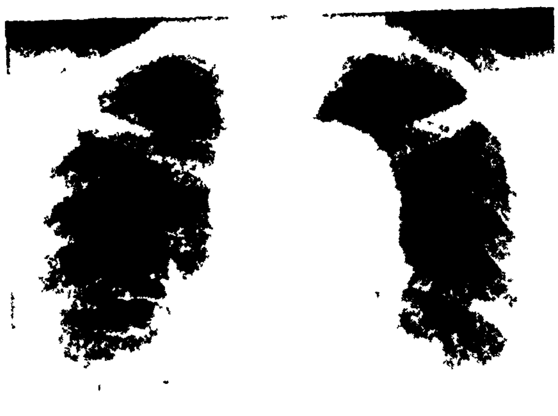

Fig. 2.—Roentgenogram of chest in first case, showing characteristic widening of supracardiac mediastinal shadow produced by dissecting aneurysm. This man, 16 years old, had a long history of hypertension.

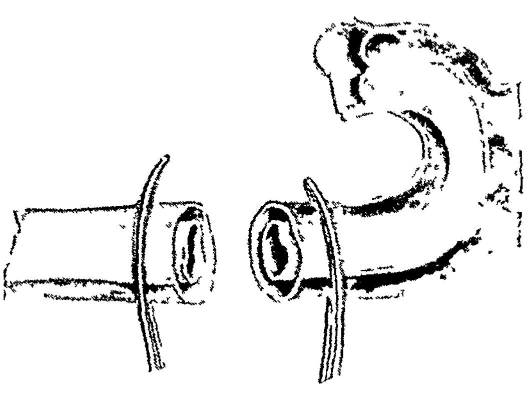

Fig. 4.—Next step in operation, cross clamping aorta and dividing it between clamps. Characteristic "double-barreled" opening representing inner true lumen and outer false lumen may be observed.

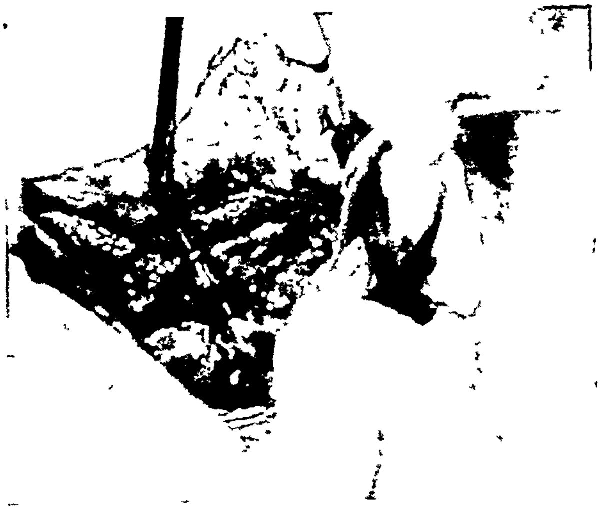

Fig. 5.—Aorta has been cross clamped and outer wall of dissecting aneurysm is being incised with scalpel as partially organized thrombus is sucked out of false lumen

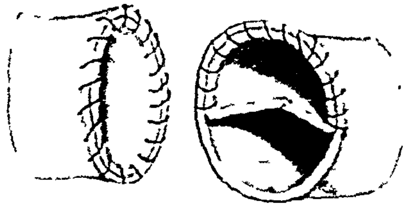

Fig 6—Approximation of inner and outer walls to obliterate false passage in lower opening of aorta and creation of a reentry passage from false to true lumen above by wedge excision of inner wall

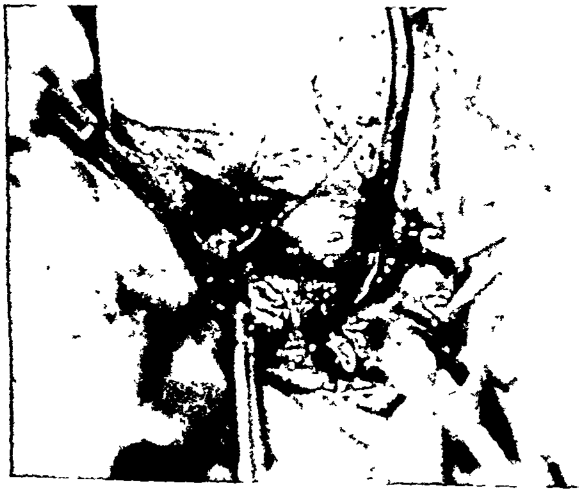

Fig 7.—Inner and outer walls of dissecting process in lower end of aorta being approximated with continuous over-and-over suture of 000 arterial silk.

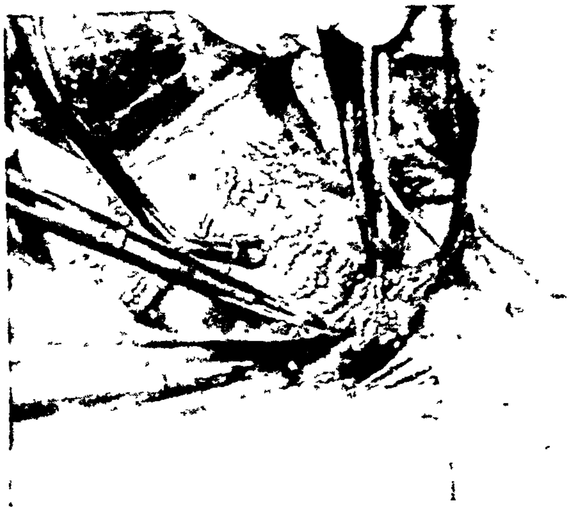

Fig 8—Wedge segment being excised from inner wall of upper end of aorta to permit reentry from dissected passage above into true lumen below

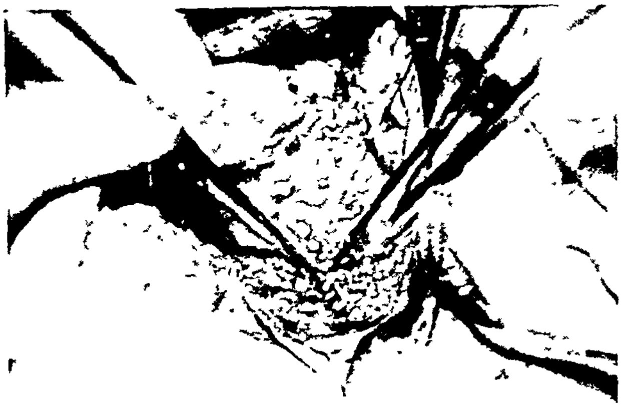

Fig. 9—Upper and lower ends of aorta approximated by end-to-end anastomosis

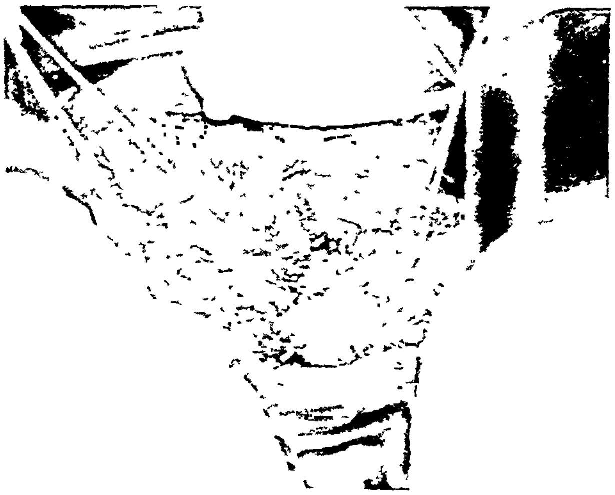

Fig 10—Anastomosis completed and occluding clamps removed, permitting restoration of aortic circulation

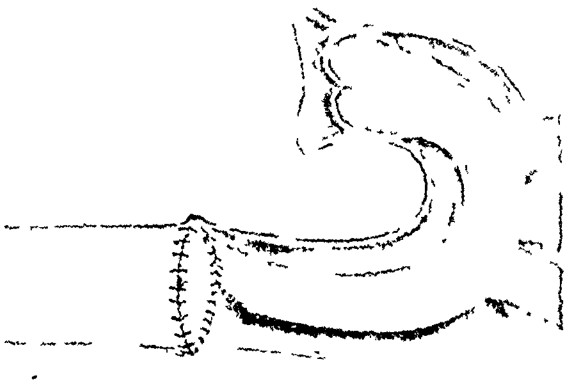

Fig. 11.—Drawing showing completed procedure and showing how blood flow is now directed from double aortic lumen above into single normal lumen below

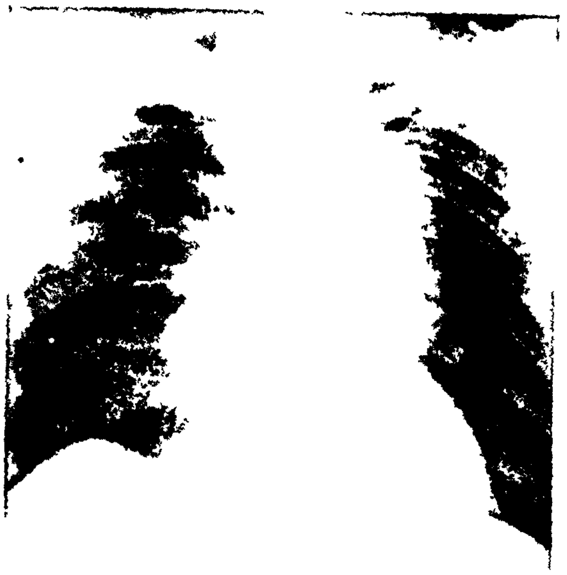

Fig. 12.—Roentgenogram in second case, showing characteristic widening of supracardiac mediastinal shadow produced by aneurysm Also present is the typical more radiolucent appearance of shadow on left side

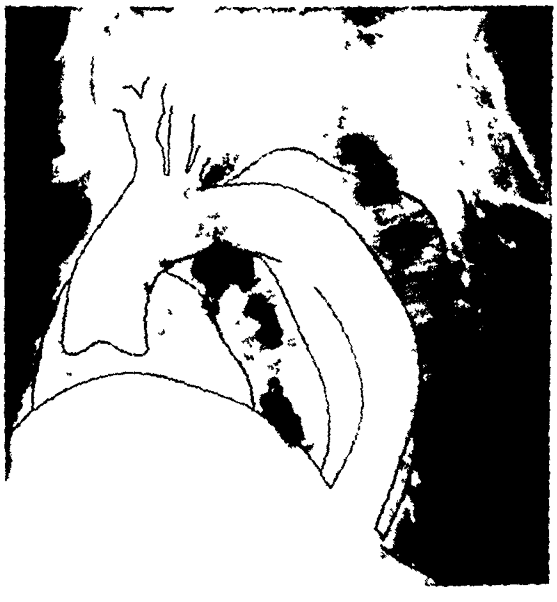

Fig. 13.—Characteristic findings of dissecting aneurysm with double aortic shadow representing true and false lumens beginning at left subclavian artery and extending throughout length of descending aorta

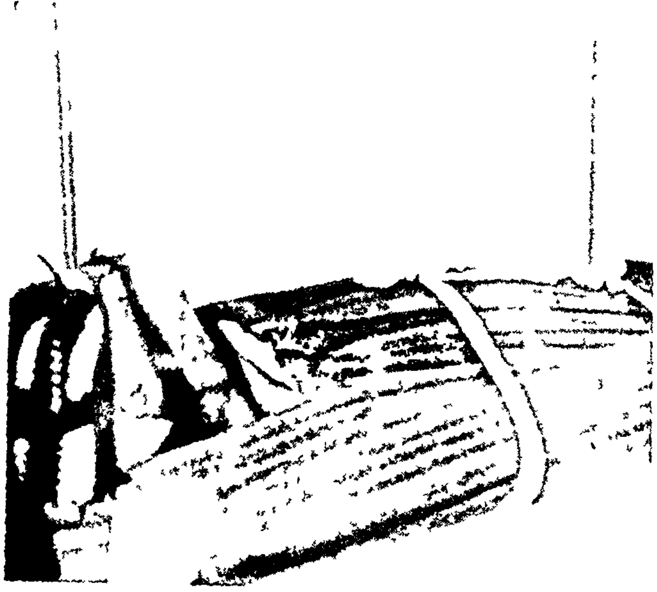

Fig. 14.—Patient has been anesthetized, and hypothermia, which is being induced, is used to protect against possible ischemic damage to spinal cord from arrest of circulation at this high level

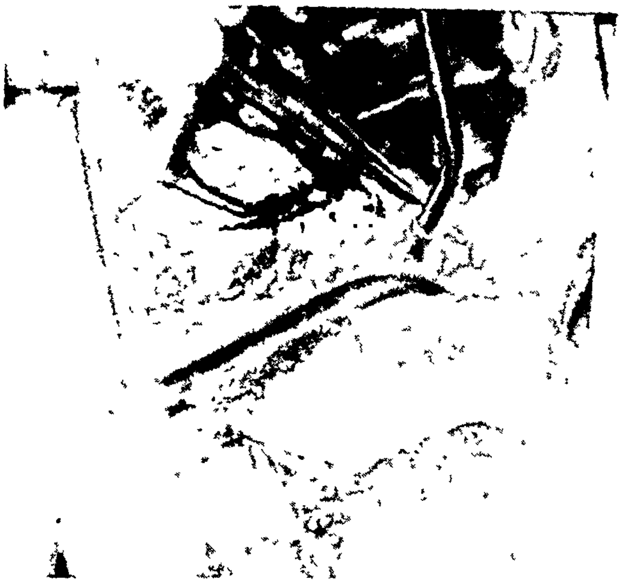

Fig. 15.—Left pleural cavity has been entered through bed of resected fifth rib. Note markedly widened segment of aorta produced by dissecting process arising near origin of left subclavian artery

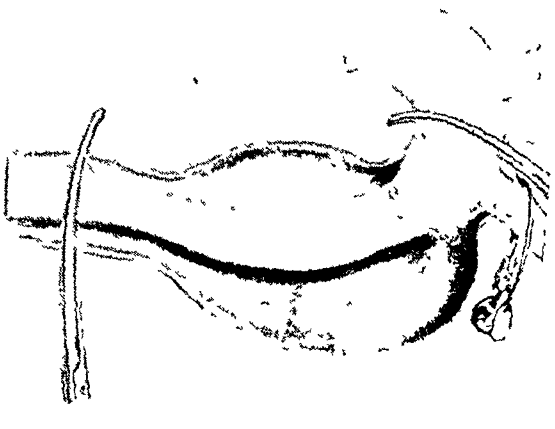

Fig. 16.—Drawing showing pathological features and next step in operation. After segment of aorta has been freed, clamps are applied to arch, left subclavian artery, and descending thoracic aorta

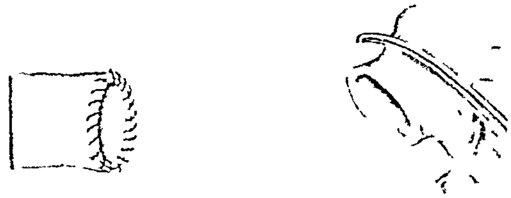

Fig 17 —Aneurysmal segment has been excised above origin of dissecting process, providing normal opening above False passage in lower end of aorta is obliterated by approximating inner and outer walls

Fig 18 —Excised segment is replaced with aortic homograft, which is being anastomosed to upper end of aorta

Fig 19 —Anastomosis of aortic homograft to upper end of aorta has been completed, and graft is being fitted for lower anastomosis

Fig 20 —Aortic homograft being anastomosed to lower end of aorta

Fig 21 —Anastomosis of aortic homograft has been completed and occluding clamps removed, permitting restoration of normal aortic lumen

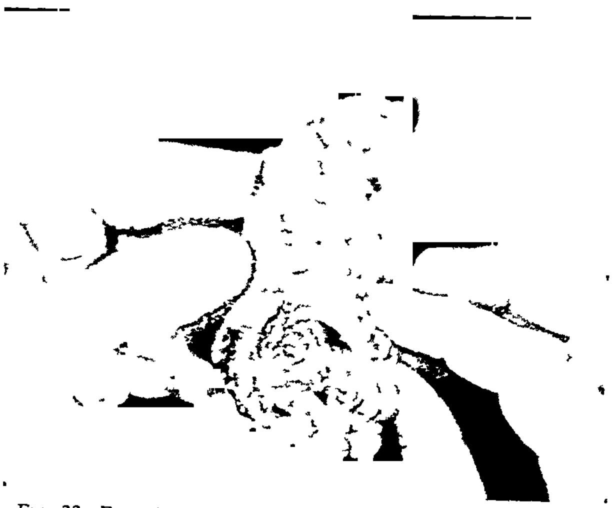

Fig 22 —Excised segment of aorta showing normal lumen markedly compressed by dissecting aneurysmal process containing partially organized thrombus

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Influence of Hot and Humid Environment on the Patient with Coronary Heart Disease. G. E. Burch. J. Chron. Dis. 4:350-363 (Oct.) 1956 [St. Louis].

That a hot and humid environment may be dangerous is evident from experiences in communities suddenly struck by a heat wave, when people of the older age groups and those with degenerative diseases are especially prone to succumb. The author reviews observations he made in studies carried out over a number of years on the influences of a hot and humid environment on the cardiovascular system. He emphasizes that such an environment can increase cardiac work as much as strenuous physical exercise. The hot and humid environment produced by climate, industrial working conditions, or overcrowding of the sickroom must be considered in the treatment of all patients in whom it is desired to reduce cardiac work. Greater use of air-conditioning in hospitals, cardiac wards, offices, and homes will assist toward this end. Many important problems concerning the influence of the hot and humid environment upon man remain unsolved and should be studied.

Acute Coronary Insufficiency: Its Differential Diagnosis and Treatment. A. M. Master, H. L. Jaffe, L. E. Field and E. Donoso. Ann. Int. Med. 45:561-581 (Oct.) 1956 [Lancaster, Pa.]

Acute coronary insufficiency is a specific clinical, electrocardiographic, and pathological entity differing from both angina pectoris and acute coronary occlusion. It indicates a more prolonged and severe myocardial ischemia than does "angina," yet does not present the characteristic electrocardiographic and laboratory features of major infarction secondary to coronary occlusion. There is no change in the heart sounds; there is no pericardial rub, heart failure, or peripheral embolization. In coronary insufficiency mild fever, slight leukocytosis, and a slight increase in sedimentation rate may appear, if significant subendocardial necrosis results. No acute thrombus is present in the coronary arteries at autopsy. The incidence of "acute coronary insufficiency" is much greater than that of coronary thrombosis. Since an attack of "acute coronary insufficiency" is rarely fatal, postmortem studies and statistics to determine its frequency are not reliable. The pathological studies that are available, particularly among Armed Forces personnel and in cases of "sudden death" in civilians, indicate that myocardial infarction occurs not infrequently without any thrombosis, i. e., as the result of "acute coronary insufficiency." Estimating that one million attacks of coronary thrombosis occur annually in the United States, the authors regard it as probable that at least 1.5 to 2 million attacks of "acute coronary insufficiency" occur each year.

Acute coronary insufficiency can develop spontaneously. Often it follows severe hemorrhage, tachycardia, marked physical exertion, emotional upset, trauma (surgical or accidental), sudden hypertension, shock, pulmonary embolism and infarction, severe infection, and heart failure. Such cases should be termed "acute coronary insufficiency" secondary to whatever the causative condition may be. Prompt treatment of the precipitating factor may terminate the resultant coronary insufficiency and may even prevent it. In acute hemorrhage, replacement of blood may be life-saving, as are vasopressor drugs in shock and hypotension. The termination of severe tachycardia is also vital. The presence of a precipitating factor in a coronary episode suggests the presence of coronary insufficiency rather than occlusion. When coronary insufficiency occurs spontaneously, it may clinically resemble coronary occlusion with mild manifestations. The electrocardiographic picture usually serves to distinguish them. The treatment of coronary insufficiency and coronary occlusion differs; hence, the recognition of the former as an entity is essential. In uncomplicated coronary insufficiency, the authors employ rest for a period of usually only one to two weeks, avoiding protracted immobilization with the accompanying hazards of peripheral thrombosis. Most patients recover and resume work within several weeks. Mural thrombi do not occur in coronary insufficiency; hence, anticoagulants need not be administered.

Influence of Oxygen Inhalation on Renal Function in Patients with Cardiac Decompensation. M. Földi, F. Soliti, E. Koltay and others. Klin. Wchnschr. 34:857-859 (Aug. 15) 1956 (In German) [Berlin, Germany].

The authors investigated the effect of oxygen inhalation on renal function in patients with cardiac decompensation. Glomerular filtration was determined with the aid of endogenic creatinine clearance; the effective quantity of plasma circulating through the kidneys was ascertained by means of PAH (*p*-aminohippuric acid) clearance; sodium was estimated with a flame photometer; and oxygen saturation of the blood was ascertained photoelectrically. After three control clearance periods (duration of a clearance period was 10 minutes) the patients inhaled for 30 minutes an oxygen–carbon dioxide-nitrogen mixture that provided 50% oxygen and 4% carbon dioxide. After this, three more clearance periods were recorded. The tests revealed that the circulatory insufficiency of cardiac decompensation is essentially due to a chronic hypoxia. This chronic hypoxia changes the renal function in the healthy organism in a manner that is identical with the renal function during cardiac decompensation. As the hypoxia is counteracted in patients with cardiac decompensation, the renal function becomes normalized, thus proving the theory that functional disturbances in the kidneys of patients with cardiac decompensation are caused by hypoxia.

Diagnostics and Therapy of Infections with Brucella Abortus and Brucella Melitensis in Man. H. Winter, W. Schmidt, G. Huels and D. Strauch. Medizinische, No. 40, pp. 1430-1434 (Oct. 6) 1956 (In German) [Stuttgart, Germany].

Thirty-seven patients with brucellosis caused by Brucella abortus and 17 patients with brucellosis caused by B. melitensis were treated with antibiotics at the medical clinic of the Justus Liebig-University of Giessen, Germany. The 54 patients, most of whom were farmers and some veterinarians, were followed up for from one to six years after their discharge from the hospital. Treatment consisted of administration of broad-spectrum antibiotics, i. e., chlortetracycline (Aureomycin), tetracycline, and oxytetracycline (Terramycin) with an initial daily dose of 2 gm., which later was reduced to 1.5 or 1 gm. A total dose of 30 gm. was given in the course of from two and a half to three weeks. Antibiotic therapy was combined recently with the administration of "stress fortification" vitamins. Erythromycin was given to two patients but was withdrawn because of its limited effect. Chloramphenicol was not used. Six of the 17 patients with brucellosis caused by B. melitensis received only broad-spectrum antibiotics, and 11 were given broad-spectrum antibiotics combined with streptomycin. A total dose of 15 gm. of streptomycin was given. Recurrences with fever were observed in 2 of the 6 patients and in 5 of the 11 patients. The recurrence ratio thus was the same in both groups. Combined antibiotic therapy thus did not prove superior to treatment with broad-spectrum antibiotics alone, which was practiced in the

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37 patients with brucellosis caused by B. abortus. Two of these patients had recurrences. The relapses occurred within a few weeks after antibiotic therapy was discontinued.

Broad-spectrum-antibiotic therapy is the method of choice for the treatment of brucellosis. The temperature is restored to normal within four or five days. The permanent success of the treatment depends on its early institution. Complete recovery, however, may be obtained only in 20 or 30% of the patients even if the treatment is instituted within the first eight weeks after the infection. Results of treatment are even less satisfactory in patients with chronic brucellosis, and it may be difficult to draw the line between recoveries resulting from treatment and tendencies to spontaneous recovery. The source of infection as a rule does not permit definite conclusions concerning the type of the Brucella infection. Cattle may serve as source of infection caused by B. melitensis, and sheep may transmit infection caused by B. abortus. Only the results of blood culture and quantitative agglutinin saturation can prove the character of the infection. This proof was obtained in 9 of the 17 patients with brucellosis caused by B. melitensis.

Histoplasmosis Contracted in Britain: A Case of Histoplasmic Lymphadenitis Following Clinical Recovery from Sarcoidosis. W. S. C. Symmers. Brit. M. J. 2:786-790 (Oct. 6) 1956 [London, England].

The author describes a case of histoplasmosis in a 46-year-old man who had never been out of the British Isles before the development of the disease. The only manifestations of the infection were the enlargement of two cervical lymph nodes and a positive skin reaction to histoplasmin. Fungi were found in sections of one of the lymph nodes. The diagnosis was established by the isolation of Histoplasma capsulatum in cultures from one node. The patient was without symptoms when last heard from, 16 months after the mycotic lymphadenitis appeared.

The patient's case is believed to be the first unequivocal instance of mycologically proved histoplasmosis in which the infection was contracted in Britain. History revealed that he had previously had sarcoidosis, the course of which was benign. At the age of 27 years he fell and cut his forehead on a path of splintered flint. The wound healed rapidly without suturing. Fourteen years later the scar became livid and indurated, forming a slowly growing, smooth linear swelling. It was excised, and sections showed a typical siliceous granuloma formed by tubercle-like structures of sarcoid type. All the manifestation of this initial illness had disappeared a year before the histoplasmic lymphadenitis developed. There is no reason to presume any relationship between the old injury in this case and the eventual occurrence of the fungal infection. It is unlikely that the original illness, believed to be sarcoidosis, was a manifestation of histoplasmosis. The absence of symptoms, the apparently complete recovery, the character of the radiological changes in the lungs and their disappearance without calcification, the clear-cut microscopic picture of sarcoidosis, and the failure to find parasites in the original biopsy specimen and in the siliceous granuloma were all features that favored the diagnosis of sarcoidosis.

Development of Resistance by Tubercle Bacteria to Various Chemotherapeutics in Combination. S. Winblad. Acta tuberc. scandinav. 32:118-131 (No. 2) 1956 (In English) [Copenhagen, Denmark].

Tubercle bacilli obtained from 865 patients with pulmonary tuberculosis who were treated at the chest clinic of the General Hospital in Malmö, Sweden, were studied systematically with regard to the development of resistance to streptomycin, isoniazid, and aminosalicylic acid. The tubercle bacilli were inoculated into Löwenstein-Jensen's medium to which varying doses of the chemotherapeutic agents had been added. The total doses of the chemotherapeutic agents that had been administered to the patients were taken into account, and so was the duration of the streptomycin and/or isoniazid therapy, which was combined with the administration of aminosalicylic acid in all the patients. Results showed that when the total dose of streptomycin exceeded 90 gm. after daily administration, more than 80% of the surviving bacteria had developed resistance to streptomycin. In a smaller group of patients who had received the same total dose of streptomycin by intermittent administration, the resulting incidence of resistance was the same. Combined treatment with streptomycin and isoniazid reduced the incidence of streptomycin-resistant strains. In patients treated with isoniazid not combined with streptomycin, the resistance of the bacteria to isoniazid was appreciable after four months of treatment. Combined treatment with streptomycin reduced the incidence of isoniazid-resistance among the surviving bacterial strains. Not until aminosalicylic acid had been administered for more than three years did the resistance of the tubercle bacilli to aminosalicylic acid become clinically important.

Tuberculous Meningitis: Combined Corticosteroid and Antimicrobial Therapy. S. J. Shane, S. E. Copp and T. K. Krzyski. Canad. M. A. J. 75:631-634 (Oct. 15) 1956 [Toronto, Canada].

Thirty patients with tuberculous meningitis were given combined treatment with streptomycin, aminosalicylic, and corticosteroid preparations at the Point Edward Hospital in Sydney, Nova Scotia, and in three other hospitals between 1953 and 1955. Hydrocortisone in an initial daily dose of 200 mg. was used as the corticosteroid of choice, rather than cortisone in an initial daily dose of 300 mg. Twenty-five patients made a complete recovery and five died. One of the five patients who died had a complete infarction of the right cerebral hemisphere that appeared to preclude recovery by any form of treatment. Two additional patients who failed to recover were admitted to hospital in so late a stage of their disease that no method of treatment could have been expected to bring about a satisfactory result. If one excludes these three patients, there remain 27 treated, 25 of whom recovered, i. e., a recovery rate of 92.6%. This recovery rate represents a distinct improvement over that in previous and current reports in the literature. Five of the 25 patients who recovered were comatose or their conditions were deteriorating or stationary when treated with streptomycin, aminosalicylic acid, and isoniazid. Dramatic clinical and laboratory evidence of improvement was noted in these patients shortly after corticosteroids were added to their therapeutic regimens.

It would seem to be clear that the addition of corticosteroids to antimicrobic regimens including isoniazid in patients with tuberculous meningitis is capable of bringing about striking improvement when the previous condition has been unsatisfactory. Neurological sequelae were distinctly less frequent in corticosteroid-treated patients than in others. There was no evidence of exacerbation of nonmeningeal tuberculosis or any evidence of the occurrence of significant intercurrent nontuberculous infections resulting from the use of corticosteroids in this disease. The corticosteroid-antimicrobic regimen in patients with tuberculous meningitis thus has advantages over antimicrobic therapy alone, even when such antimicrobic therapy includes isoniazid.

Some Quantitative Aspects of Treatment with Quinidine. M. Sokolow. Ann. Int. Med. 45:582-588 (Oct.) 1956 [Lancaster, Pa.]

The customary reliance on quinidine dosage is less satisfactory than the determination of the concentration of quinidine in the blood. Quinidine can be determined in the blood because it fluoresces in acid media, and the degree of this fluorescence can be measured in a Coleman fluorometer. Serum concentration of quinidine determines both the conversion of an arrhythmia as well as toxicity. Toxic reactions rarely result from true sensitivity or idiosyncrasy manifested by fever, purpura, rashes, or hypotension. A test dose of 0.2 gm. of quinidine is advisable before starting treatment, in order to determine possible idiosyncrasy. Other signs of mild or moderate quinidine intoxication consisting chiefly of nausea, diarrhea, and occasionally of headache or tinnitus rarely require the cessation of treatment with quinidine. The gastrointestinal disorder can be controlled by sedatives, paregoric, or thorazine. When signs of myocardial intoxication are present, such as frequent ventricular premature beats (one or more every six beats), an increase of QRS width of 50% or more, complete AV block, ventricular tachycardia, or ventricular fibrillation, the author usually discontinues treatment with quinidine. In about

700 serum determinations it was found that only three cases of myocardial toxic reaction had occurred at serum levels less than 6 mcg. per milliliter, and none at less than 3 mcg. per milliliter. The incidence of myocardial toxicity increased progressively as the serum concentration exceeded 6 mcg. per milliliter; it rose to 65% at levels over 14 mcg.

The conversion of chronic auricular fibrillation to sinus rhythm by the use of quinidine was studied in 214 conversion attempts in 177 patients. Conversion was attempted by one of two techniques: (1) the rapid method—0.4 gm. every two hours for five doses, repeated the next day, then increased to 0.6 gm. every two hours for five doses if warranted by the patient's response and the absence of toxic reaction; and (2) the slow method—0.4 gm. four times a day for 72 hours, increased to 0.6 gm. four times a day for 72 hours, and then to 0.8 gm., depending upon the response and lack of toxic effect. Factors having an adverse effect on conversion were rheumatic etiology; duration of fibrillation longer than six months, and especially longer than a year; the presence of cardiac failure that did not respond to the usual measures of therapy; and mitral insufficiency. The conversion rate was approximately 75%, but it varied from 95% in patients without cardiac failure and with fibrillation of short duration to approximately 45% in patients with mitral regurgitation, with or without cardiac failure. Determination of quinidine concentration in the serum should decrease the risk of toxicity to the patient and permit safer and more effective therapy.

Treatment of Acute Pancreatitis with Cortisone. N. C. Rogers, A. O. Wilson, M. J. Meynell and W. T. Cooke. Lancet 2:651-652 (Sept. 29) 1956 [London, England].

The authors present observations on six patients with acute pancreatitis who were given cortisone in addition to the usual supportive measures. All recovered. The authors gained the impression that cortisone therapy favorably influenced the rate of recovery. The patients who were operated on were usually given an intramuscular injection of hydrocortisone after the operation, and, thereafter, prednisone was given by mouth in addition to antibiotics, fluids intravenously, and other measures. Patients not operated on were given prednisone by mouth together with other treatment. Two of the six patients had especially severe forms of pancreatitis. The authors feel that these two probably would have died without the use of cortisone, the more so since they had observed four successive deaths from necrosis of the pancreas before they resorted to the use of cortisone.

Gamma Globulin Deficiency: Report of a Case and Survey of Literature. A. H. Greenhouse. J. Kansas M. Soc. 57:611-618 (Oct.) 1956 [Topeka, Kan.].

The patient was a 58-year-old man recently observed at the University of Kansas Medical Center. He had repeated bouts of fever. Electrophoretic studies of his blood failed to show the presence of gamma globulin. Hematological studies did not reveal isohemagglutinins. Typhoid immunization was attempted, and he responded to each injection with a marked temperature spike, but repeated studies failed to reveal any agglutinins to typhoid. The patient was febrile during the early part of his hospital stay until he was given an injection of 20 cc. of gamma globulin, at which time his temperature subsided almost dramatically. He remained afebrile except for the temperature elevations with typhoid immunization and felt well on discharge from the hospital. Since then he has been followed in the Kansas University Medical Center outpatient clinic and has had a few febrile bouts, each of which responded promptly to gamma globulin injections.

The literature on agammaglobulinemia suggests that it is probably not a rare condition. The following features should raise the suspicion of agammaglobulinemia: (1) grossly inadequate resistance to infection, as manifested by frequently recurring and unusually severe infections; (2) failure to develop clinical immunity after a seemingly adequate antigenic stimulus, such as repeated attacks of a disease usually conferring permanent immunity; and (3) certain laboratory findings. Treatment consists of replacement of gamma globulin.

Urinary Gonadotrophin Excretion in Osteoarthritis. F. B. Rogers. Am. J. M. Sc. 232:419-420 (Oct.) 1956 [Philadelphia].

The authors observed a patient with arthritis mutilans, in whom the cartilaginous lesions had repeatedly flared up after the injudicious administration of chorionic gonadotropins. Since cartilage destruction occurs in both osteoarthritis and arthritis mutilans, it seemed worthwhile to find whether osteoarthritic patients showed excess gonadotropin excretion. Ten postmenopausal patients were selected who had osteoarthritis involving the proximal and distal interphalangeal and other joints. Pituitary gonadotropin excretion was almost identical in the 10 patients with osteoarthritis and in 10 matched controls. It may, therefore, be assumed that the amount of gonadotropins, as measured by current techniques, is not a factor in the causation of osteoarthritis.

Staphylococcal Gastroenteritis: Report of a Major Outbreak. H. Wain and P. A. Blackstone. Am. J. Digest. Dis. 1:424-429 (Oct.) 1956 [New York].

Symptoms of food poisoning appeared in 244 of 306 persons attending a picnic. The offending food was baked ham from which cultures of Micrococcus (Staphylococcus) aureus were obtained by two separate laboratories. The baked ham presented no off-odors, tastes, or flavors. This is characteristic of foods infected with micrococci. It was established that the baked ham was seeded with M. aureus from the self-contaminated hands of the man who did the deboning. Laboratory cultures demonstrated M. aureus in acne lesions on the man's face, in the ham, and in scrapings taken from the table on which the hams were deboned. The micrococci organisms were given the necessary time and temperature range in which to grow and produce enterotoxin in the sliced ham during the period that the hams were held warm in the oven at 200 F. Additional growth and enterotoxin production occurred during the period that the hams were held without refrigeration at the picnic grounds, on a day when the temperature was 90 F. The characteristic feature of micrococcic gastroenteritis is the relatively short incubation period, which is usually one to six hours. This is in contrast to incubation periods of 12 to 24 hours or more in botulism or poisoning due to Salmonella. This point is of importance in diagnosis, both clinically and epidemiologically, because if the incubation period is longer than 11 hours, micrococcic gastroenteritis can be ruled out.

The majority of the patients recovered in from 24 to 72 hours. Several patients were hospitalized as long as five days. One individual who had a long history of ulcerative colitis had severe bleeding from the mouth and anus and needed 2 pt. of blood. It is important that all food handlers receive a daily inspection and that no employe be permitted to come in contact with food who has an uncovered open sore or obvious infection. This outbreak could have been prevented had this been done. However, because of the ubiquity of carriers of Micrococcus organisms and the impracticability of eliminating them from food handling, all foods must be properly handled and stored. Food must be kept constantly hot, properly refrigerated, or promptly eaten. Reheating of food requires at least 30 minutes at 350 F to effectively inactivate any enterotoxin that may have contaminated it.

Hodgkin's Disease and Caseous Tuberculosis (With Report of a Case). E. H. Horton. Brit. J. Tuberc. 50:365-367 (Oct.) 1956 [London, England].

Horton reports on a 56-year-old woman with enlarged left supraclavicular lymph nodes. One of these was excised, and biopsy showed caseous tuberculosis. She was treated with streptomycin and isonicotinic acid hydrazide but failed to improve and soon became wasted and anemic. She also had symptoms of an abdominal nature, and marked enlargement of liver and spleen was noted. Death ultimately occurred from hepatic failure thought to be due to tuberculous involvment of the liver. Diagnosis of Hodgkin's disease was not made in this case until death had occurred. It had been considered in differential diagnosis, but the discovery of caseous tuberculous lesions in the cervical lymph node biopsy was always the overriding consideration. Also, the high alkaline phosphatase value recorded at one stage of the illness suggested the possibility of biliary obstruction caused by enlarged tuberculous lymph nodes in the portal fissure. At autopsy the hepatic enlargement was found to be due to Hodgkin's disease. Microscopic examination of the enlarged cervical nodes showed the classic picture of Hodgkin's infiltration on the one hand and caseous tuberculosis on the other. Different areas of the same lymph node exhibited this feature. No tubercle bacilli were demonstrated. This case illustrates the extremely close relationship that exists between these two conditions. If this had been appreciated, the true nature of the condition that ultimately caused death might well have been realized during the course of the illness by further microscopic examination of the cervical lymph nodes. In the light of the clinical course, too much significance was attached to the single biopsy report.

The Long-Term Results of the Treatment of Pulmonary Tuberculosis by Pneumoperitoneum. A. Pines. Brit. J. Tuberc. 50:338-345 (Oct.) 1956 [London, England].

A follow-up of at least six and a half years was deemed necessary to evaluate the long-term results of pneumoperitoneum in the treatment of tuberculosis. The years chosen for analysis, therefore, were 1945 to 1947, when pneumoperitoneum was in maximal use at the author's (Harefield) hospital. Streptomycin was not used initially in any of these patients and in comparatively few during after-years. All patients who received primary pneumoperitoneum treatment were included and also those in whom a pneumothorax had been tried but had failed and had been promptly abandoned. The pneumoperitoneum had been maintained in all of these patients for at least three months. Of 334 patients who had been treated with pneumoperitoneum, 287 could be traced; in 225 adequate data were available. Fifty-nine (26%) of the patients had died by the end of the observation period. In relation to extent of disease, 17% of those who had moderately advanced disease died, as did 57% of those who had far-advanced lesions. These results were compared with the published results in patients treated largely by bed rest alone in relation to comparable extents of disease. There was little or no significant difference in their ultimate fate. Pneumoperitoneum treatment, therefore, had little demonstrable effect upon survival in this series of patients. It is not, consequently, a primary treatment of value in pulmonary tuberculosis.

The Efficacy of BCG Vaccination: Epidemic of Tuberculosis in a State School, with an Observation Period of 12 Years. T. V. Hyge. Acta tuberc. scandinav. 32:89-107 (No. 2) 1956 (In English) [Copenhagen, Denmark].

An epidemic of tuberculosis occurred in a Danish State school for girls in the first three months of 1943. This epidemic fulfilled most of the requirements of a controlled experiment concerning BCG vaccination. The 368 girls who attended the school at the time of the epidemic were followed up for more than 12 years. At the annual examination for tuberculosis in December, 1942, which preceded the outbreak of the epidemic, Mantoux tuberculin tests were performed on 368 girls; 105 had a negative reaction to the test, 133 had a positive reaction after BCG vaccination, and 130 had a spontaneous positive reaction. Thus 263 girls were tuberculin-positive. Most of the tuberculin-negative pupils were newcomers to the school, and it was not possible to have them vaccinated before the outbreak of the epidemic. Ninety-four of the 105 girls were exposed to the infection. Seventy of the 94 turned from tuberculin-negative to tuberculin-positive. Forty-one convertors showed evidence of primary tuberculosis. Postprimary progressive pulmonary tuberculosis occurred in 14 convertors (15% of the 94 exposed girls) after a latent period of up to 10 years. Of the 133 BCG-vaccinated girls, 106 were exposed to the infection under the same conditions as the tuberculin-negative girls. None of these showed evidence of primary tuberculosis, and postprimary progressive pulmonary tuberculosis occurred in only two (1.9% of the exposed). There were, therefore, eight times as many cases of postprimary pulmonary tuberculosis in the tuberculin-negative group as in the BCG-vaccinated group; the total incidence of primary and postprimary tuberculosis was 23 times as high among the tuberculin-negative as among the BCG-vaccinated pupils. Of the 130 pupils with a spontaneous positive reaction to tuberculin, 105 were exposed to the infection: progressive pulmonary tuberculosis occurred in 10 of the 105 after a latent period of up to more than eight years.

Twenty-four cases of postprimary progressive pulmonary tuberculosis thus occurred in the initially tuberculin-negative and tuberculin-positive groups as compared with only two cases in the BCG-vaccinated group. It is evident that the person most effectively protected against tuberculous infection is the non-reactor who is properly vaccinated with a potent BCG vaccine that produces strong and lasting allergy.

Considerations on 53 Cases of Malignant Lymphogranulomatosis with Attention to Tubercular Reactions of the Skin. A. Zurlo and G. Greco. Sett. Med. 44:375-380 (July 31) 1956 (In Italian) [Florence, Italy].

The authors report on 53 patients with malignant lymphogranulomatosis, as ascertained by biopsy. There were 34 males and 19 females. Their ages ranged between 11 and 67 years. The symptoms had been present for from one month to 11 years. Eleven of the 53 patients returned two, three, or four times for observation during relapses. Twenty-two patients presented a positive Mantoux test. Seven of these had had tuberculosis and two had relatives with tuberculosis. The initial localization of the disease was most frequently in the lateral cervical regions (28 of 53 patients). Other locations were mediastinum, 58 patients; supraclavicular region, 3 patients; axillary region, 5 patients; and inguinal region, 3 patients. The number of leukocytes in peripheral circulation was above 8,000 per cubic millimeter. Eight patients who had had the disease for four months or less had a leukocyte count of 8,737 per cubic millimeter. Neutrophilia and lymphocytopenia were present in 27 patients (50.94%). Eosinophilia with values higher than normal was present in 13 patients (24.52%). Marked splenomegaly was present in 14 patients (26.41%). Itching was present at the beginning in only 12 patients (22.64%). Apparently there was no relationship between itching and tuberculin intradermal reaction. High fever was present in 20 patients (37.73%), all of whom had had the disease for at least a year; low fever was present in 24 patients (45.28%). Nine patients had no fever when they entered the hospital. The authors conclude that a positive Mantoux test in patients with lymphogranulomatosis depends upon previous tuberculous infection and on the condition of the patient during the initial stage of the disease, when the reactivity of the tissues is still present.

The Treatment and Prognosis of Hepatic Coma. S. Sherlock, W. H. J. Summerskill and A. M. Dawson. Lancet 2:689-694 (Oct. 6) 1956 [London, England].

The authors report observations on the treatment of 66 consecutive patients (41 females and 25 males) with liver disease complicated by hepatic coma or precoma. Diagnosis was based on clinical findings and serial biochemical tests and was confirmed in 18 by aspiration biopsy of the liver and in 27 others at autopsy. The majority of the patients (47) had hepatic cirrhosis, 13 had virus hepatitis, and 6 had miscellaneous disorders. The neuropsychiatric syndrome consists of progressive impairment of emotional control and intellect, the patient passing from stupor into coma. Common motor system signs are a "flapping tremor" of the outstretched hands and increased muscle tone, with hyperreflexia and ankle clonus. The treatment described is based on the concept that toxic nitrogenous substances of intestinal origin can be incriminated in the pathogenesis of hepatic coma. The intestines were emptied and kept free of all nitrogen-containing material. All dietary protein was stopped, and at least 1,600 calories were supplied daily as glucose drinks or as a 20% glucose solution through an intragastric drip. When necessary, a 40% dextrose solution was given intravenously via an antecubital vein into the innominate vein or superior vena cava, since small veins would be thrombosed by dextrose of this strength. Care was taken to avoid fluid overload. Chlortetracycline was given, and any precipitating factor was energetically treated.

Thirty-nine of the 66 patients recovered, 21 of the survivors having been in acute deep coma. Sodium glutamate was given intravenously on 12 occasions without clinical improvement. Thirteen patients with chronic neuropsychiatric changes (chronic portal-systemic encephalopathy) were maintained on low-protein diets for from 2 to 24 months without showing signs of protein malnutrition, and the serum albumin levels were well maintained. The prognosis was better in cirrhosis than in acute virus hepatitis and also if treatment was initiated in the precomatose stage. Outlook was also better when a clear precipitating factor, such as gastrointestinal hemorrhage, was amenable to therapy. In cirrhotic patients, when coma was associated with signs of liver failure such as ascites, jaundice, or a low serum-albumin value the prognosis was bad. When patients with acute hepatitis survived, they usually recovered completely. Seven of eight patients with cirrhosis who survived deep coma were alive a year later.

Thymectomy During Respiratory Failure in a Case of Myopathy with Myasthenia Gravis. S. G. Griffin, F. J. Nattrass and E. A. Pask. Lancet 2:704-707 (Oct. 6) 1956 [London, England].

The patient described presented an unusual myopathic picture, which, at the age of 35, was complicated by severe myasthenia, including virtually complete respiratory failure. Artificial respiration was maintained for several weeks, but it proved impossible to secure the return of breathing by the use of the usual antimyasthenic drugs. Eventually thymectomy was done while the patient was still in respiratory failure, and after the operation full respiratory power returned. The patient recovered to a condition as good as, or slightly better than, that which prevailed before the crisis, and he no longer requires neostigmine.

SURGERY

Complications of Thyroid Surgery. O. H. Beahrs, R. F. Ryan and R. A. White. J. Clin. Endocrinol. 16:1456-1469 (Nov.) 1956 [Springfield, Ill.].

Between 1940 and 1955, 14,374 thyroidectomies were performed at the Mayo Clinic. Thirty-seven (0.7%) of 5,402 patients undergoing thyroidectomy between 1940 and 1945 died at the hospital as compared with 9 (0.1%) of 8,972 patients who were operated on between 1946 and 1955. The obvious reduction of the death rate was the result of more careful selection of patients and the availability of antibiotic agents. The complications of thyroid surgery were reviewed for the year 1954, in the course of which 1,021 thyroidectomies were performed. The incidence of unintentional paralysis of the vocal cords was 1.3%. Tetany, which was not anticipated, occurred in only 0.2% of patients undergoing primary thyroid operation for benign goiter. Myxedema occurred postoperatively in at least 30% of the patients with thyroiditis. The only other significant complications consisted of hemorrhage in two patients, toxic psychosis in one, obstruction of the airway in two, and cardiac arrest in one. Fifteen tracheotomies were established prophylactically or as emergency procedures to alleviate airway problems.

Pericardiectomy for Chronic Idiopathic Pericarditis with Massive Effusion and Cardiac Tamponade. H. B. Shumacker Jr. and J. Harris. Surg. Gynec. & Obst. 103:535-538 (Nov.) 1956 [Chicago].

Chronic idiopathic pericarditis with massive effusion and cardiac tamponade may exist for long periods of time and may eventuate in chronic constrictive pericarditis. Its early management by extensive pericardiectomy is a relatively new concept. The authors cite the cases of two patients with massive effusion and cardiac tamponade who were effectively treated by extensive pericardiectomy. Patients with chronic idiopathic pericarditis with massive effusion and cardiac tamponade should be treated surgically at an early date. Though three reported patients treated by pericardiopleural fenestration did well, the authors feel that extensive pericardiectomy is the preferable procedure. The operation is technically easy, and the entire anterior and lateral surfaces of the pericardium can be excised. Such treatment removes the major portion of the primary disease. It brings to an early end the disabling consequences of cardiac constriction. It prevents the long-continued tamponade with its potentials for permanent myocardial damage. It eliminates the necessity of performing pericardiectomy later during the phase of constrictive pericarditis, when the operation is technically more difficult and somewhat more hazardous

Leiomyoma of the Jejunum with Hemorrhage. R. L. Bradley, E. H. Short and M. M. Klein. Radiology 67:576-577 (Oct.) 1956 [Syracuse, N. Y.].

The authors cite the case of a 74-year-old man in whom a smooth muscle tumor of the proximal jejunum, with a 6-cm. segment of intestine and its mesentery was resected. Smooth muscle tumors of the gastrointestinal tract are uncommon, and, in the absence of metastases, distinction between benign and malignant forms cannot be made grossly. Histologically, the presence of two or more mitotic figures per high-power field and poor differentiation indicate malignancy. The malignant tumors usually grow slowly and metastasize late. Surgical excision is the treatment of choice and affords a high percentage of cures. These tumors may be subserosal, intramural, or submucosal. The submucosal lesions may ulcerate and bleed or may lead to intussusception. When occurring in the duodenum, they mimic duodenal ulcer, with pain, spasm, and bleeding.

Circulatory Arrest After Profuse Hemorrhage with Special Regard to After-Treatment. I. H. Rygg and P. N. Pedersen. Nord med. 56:1275-1277 (Sept. 6) 1956 (In Danish) [Stockholm, Sweden].

Long-continued complete circulatory arrest occurred in a man aged 55 after profuse hemorrhage due to the severing of the ligature on the pulmonary artery shortly after the completion of left pneumonectomy. The chest was reentered and the pulmonary artery clamped, and the patient was resuscitated by cardiac massage and by rapidly instituted blood transfusion. He remained comatose for two days, after which improvement set in. There was grave psychic impairment without focal symptoms apart from left-sided paresis of the recurrent nerve as a result of the operation. Ambulant control four and a half months after the operation showed definite psychic improvement, Goldstein and Rohrschach tests indicated only slight psychic impairment of a focal type. The value in such cases of postoperative treatment consisting of oxygen therapy, induced hypothermia, and high intake of vitamins B, C, and E is stressed. If the patient can be brought through the acute stage, slow regression of the symptoms during the first year or years is seen. Decerebration, rigidity, and coma lasting over four days are unfavorable prognostic signs. In the case in question the prognosis ought to be relatively good with reference to the hypoxic injuries, as there has been steady improvement in vision, psychic condition, and the electrocardiogram.

Prevention and Control of Postoperative Wound Infections Owing to Staphylococcus Aureus. C. W. Howe. New England J Med. 255:787-794 (Oct. 25) 1956 [Boston].

The problem of wound infection caused by Micrococcus (Staphylococcus) pyogenes var. aureus has always been a prominent component of the over-all picture of surgical sepsis The extensive use of antibiotics in a hospital, by virtue of the emergence and dissemination of resistant strains, may intensify this problem to such an extent that the over-all infection rate is increased. This appears to have been the case in the Massachusetts Memorial Hospitals between 1949 and 1953. During the latter part of 1953 and early 1954 various measures to prevent cross contamination and the dissemination of antibiotic-resistant bacteria were inaugurated. Routine antibiotic prophlaxis on the house service was abandoned late in 1953 and by the middle of 1954 had been largely curtailed on the private service. The use of antibiotics was reduced to a minimum, being limited to treatment of established infections. It was recommended that bacteriological cultures be taken before giving an antibiotic, especially for patients with chronic or mixed infections or both. Micrococcic infections were treated with an appropriate combination of antibiotics. Since the nasopharynx is the natural reservoir for the Micrococcus, it was urged that two face masks, one over the other, be worn during operations and that they be changed by the circulating nurse every hour and a half during long procedures. A full 10-minute surgical scrub with a G-11 soap, at least for the first case, was advocated. Established principles of meticulous abdominal preparations, gentle atraumatic techniques, dry wounds, and careful closure were emphasized. Preventive measures on the wards consisted of the use of face masks for doctors, nurses, and patients and the use of gloves during the changing of septic dressings to help prevent the personnel from becoming carriers. Special septic sets were used containing the necessary instruments in an aluminum pan covered by a large, sterile, double-ply cloth wrapper. The set was unwrapped at the bedside, and at the conclusion of the dressing instruments, gloves, and other contaminated materials were deposited in the pan, which was then rewrapped and sent for autoclaving before cleaning and definite sterilization. Strict aseptic technique was applied to the dressing truck. Local isolation of infected wounds by impermeable occlusive dressings and of the nasopharynx and skin by masks and gloves proved feasible. Conversion of an infected wound into a clean one by immediate drainage and débridement under proper antibiotic protection was performed when possible, allowing early secondary closure.

Comparison of postoperative wound infection rates in surgical floor and operating-room patients in 1953, 1954, and 1955, and comparison of hospital carrier rates for M. pyogenes in the house surgical floor and operating room patients and personnel in August, 1953, and in August. 1955, showed that during the last two years the hospital carrier rate of Micrococcus and the incidence of penicillin-resistant strains in carriers have been significantly lowered, and the rate of postoperative wound infections has been reduced by almost half since the institution of the relatively simple program for the prevention of crosscontamination and judicious use of antibiotics. The prophylactic administration of antibiotics in civilian surgery is reasonable and helpful under certain circumstances, but the indications are limited and need further clarification. When adopted as a routine measure before and after all "clean" operations, it may be more harmful than beneficial. Emphasis is placed on well-established surgical and antiseptic techniques rather than prophylactic antimicrobial therapy.

Gastric Carcinoma in Identical Twin Women. G. A. Spikes, W. H. Yates, H. G. Liberty and H. Renger. A. M. A. Arch. Surg. 73:733-736 (Nov.) 1956 [Chicago].

The authors describe two fatal cases of cancer of the stomach in monozygotic twin women aged 66 and 67 in whom the tumor was apparently present simultaneously, although the symptoms began and the deaths occurred nearly a year apart. The cancers were not identical histologically, but both were adenocarcinomas arising in the gastric mucosa. The patients were considered monozygotic on the basis of their statements that they were often confused even by members of their own family and that their thinking and personalities were nearly identical. Their blood types were the same. Their heights and weights were almost identical. Coloring of the hair and eyes and general configuration of the face, ears, hands, and feet were the same. An exploratory laparotomy was performed in both patients and revealed an extensive neoplasm of the stomach that was not resectable. The diagnosis was established by biopsy of a large lymph node from the greater curvature of one patient and by biopsies of nodes from the greater omentum, the liver, and a wedge from the anterior stomach wall of the other patient. It seems doubtful that earlier diagnosis or suspicion of carcinoma in the second twin could have altered the outcome.

It has been stressed by some that tumors in identical twins occur at more nearly the same time, more often in the same place, and with more certainty than in nonidentical twins. It is by reason of this simultaneous occurrence that this knowledge will be of little help in treatment of carcinoma of the stomach, since by the time it is diagnosable it is often incurable. Only one other pair of identical twins dying of carcinoma of the stomach has been reported in the American literature; two pairs of twins with cancer of the stomach have been reported in the European literature. In the United States gastric carcinoma may reasonably be estimated to cause 50,000 deaths per year. About one person in 150 is an identical twin. Consequently, if there are no determinants save chance, over 300 identical twins should die in the United States annually from gastric carcinoma. Carcinoma of the stomach occurred in only one twin of each of the two pairs of identical twins whose cases were collected from the European literature; the other twins were unaffected for 16 and 7 years respectively. The presented evidence tempers the older concept that monozygous twins must necessarily have simultaneous identical tumors. While a general predisposition might lead to tumors in each of a pair of twins, it could not explain their identical location or simultaneous occurrence.

Giant-Cell Tumors of Bones. C. Zuckermann. Rev. mex. cir. ginec. y can. 24:195-216 (July) 1956 (In Spanish) [Mexico, D. F., Mexico].

Multinuclear giant-cell tumors of the bones are, as a rule, benign, but they may be cancerous and produce metastases. Tumors of this kind develop selectively on the epiphyses, mainly those of the femur, tibia, radius, and humerus. They also develop on the maxilla and the bones of the cranium, the hands, and the feet. They constitute 20% of all tumors of the bones. They are huge, rapidly recurring, do not respond to treatment, and cause fractures and local destruction of bone. The early symptoms consist of subacute local pain and moderate changes in the bone, which can be visualized by roentgen examination, disclosing the roentgen picture of osteolysis. The diagnosis is made by clinical and roentgen examination and biopsy. The tumors can be differentiated from bone cysts, parathyroid osteosis, osteosarcoma, osseous metastases of cancer, and osseous eosinophilic granuloma. The treatment consists of roentgen therapy or surgery (resection of the tumor segment of the bone or amputation). Ten patients were observed. The tumor was cancerous in two and benign in eight. Treatment of cancerous tumors consisted of disarticulation of the hip joint in one patient and of amputation of the thigh in another. In the eight cases of benign tumor the treatment consisted of amputation in two, segmental resection in three, and roentgen therapy in three. Amputation was resorted to in a patient with a huge femoral tumor and in another with a recurrent tumor of the tibia.

Dermatome Débridement and Early Grafting of Extensive Third Degree Burns in Children. I. A. Meeker Jr. and W. H. Snyder Jr. Surg. Gynec. & Obst. 103:527-534 (Nov.) 1956 [Chicago].

During the 18-month period from September, 1954, to April, 1956, 13 children with third-degree burns covering from 15 to 65% of the total body surface were admitted to the Los Angeles Children's Hospital. The areas of full-thickness burn injury were débrided in stages with an electric dermatome. This new technique of dermatome débridement in extensive third-degree burns permitted early grafting and more rapid wound closure and resulted in a more than 60% reduction in the length of hospitalization. It was achieved without incurring massive blood loss or inadvertently destroying viable skin, as has occurred with other forms of surgical débridement. To protect against serious wound infection, bacteriostatic dressings employing tetracycline hydrochloride were applied continuously during all phases of treatment until complete epithelization of the wound had taken place.

It is practical to manage major third-degree burn injuries from the onset by a series of planned, staged surgical procedures involving dermatome débridement and subsequent early grafting. Dermatome débridement has proved to be a safe, satisfactory technique for removing extensive burn eschar. When such débridement is followed by early extensive grafting, the patient's pain and suffering is immeasurably reduced, the care of the patient is simplified for the surgical and hospital staffs, and the period of hospitalization is shortened. It is estimated that 840 days (or 2.3 years) of hospitalization were saved in 12 children with severe burns who were treated with dermatome débridement instead of by standard methods.

A Twenty Year Follow-Up in Fifty Below Knee Amputations for Gangrene. B. C. Smith. Surg. Gynec. & Obst. 103:625-630 (Nov.) 1956 [Chicago].

Smith has used a modified guillotine amputation below the knee for gangrene of the extremity in patients with diabetes and arteriosclerosis since 1930, primarily because of the advantages of preserving the function of the knee-joint and because of the poor results obtained with amputations through the thigh. He describes his technique of the below-the-knee amputation and reviews the results in 50 patients. Six of them died in the hospital; 5 lived less than a year; 17 died between 1 and 5 years after operation; 9 survived from 5 to 10 years and 6 for 10 to 15 years; 5 lived over 15 years; and the remaining 2 could not be traced. The average survival was five and one-half years, and 81.2% of the stumps were suitable for prostheses. The large number rehabilitated to full-time or part-time work, the mortality of 12% (which should be improved with more careful selection of cases), the reamputation rate of 6%, and the fact that 42% of bilateral amputees are using artificial legs constitute factors sufficiently encouraging to warrant the abolition from textbooks and from teaching institutions of the doctrine that thigh amputation is the method of choice in such patients.

Periodic Benign Synovitis: Idiopathic Intermittent Hydrarthrosis. A. D. Weiner and R. K. Ghormley. J. Bone & Joint Surg. 38-A:1039-1055 (Oct.) 1956 [Boston].

Periodic benign synovitis is characterized by the regular cyclic recurrence of articular pain, swelling, or limitation of motion without permanent deformity of the joint or injury to the bone. The common features, general pattern, and response to therapy of this disease for which various other terms, and among them idiopathic intermittent hydrarthrosis, had been suggested were studied in 14 male and 33 female patients between the ages of 13 and 45 years. They were selected from 1,800 patients seen at the Mayo Clinic between 1930 and 1954 by using the following diagnostic criteria: recurrence of articular symptoms at regular intervals; complete freedom from signs and symptoms between attacks; absence of systemic reaction; and absence of a specific causative factor that would account for the articular symptoms, i. e., bacteria, rheumatic fever, trauma, and purpura. Although one or both knees were involved in 40 of the 47 patients, any peripheral joint may be involved with the disease.

Specimens of synovial membrane were obtained from the knees of 10 patients by needle biopsy or surgical incision. Microscopic examination of these specimens revealed a picture similar to that seen in cases of rheumatoid synovitis. The villi were edematous to a greater or lesser degree and were hyperemic. The vessels in the villi appeared somewhat dilated and occasionally had thickened walls. Occasionally the synovial membrane and villi were markedly infiltrated with plasma cells and lymphocytes. The cellular infiltration was sometimes focal and confined to perivascular regions and other times was diffuse. Workers who consider this microscopic picture as pathognomonic of rheumatoid arthritis may conclude that periodic benign synovitis is a rare form of rheumatoid synovitis; those who consider this histological reaction as a nonspecific one may favor the concept that periodic benign synovitis is a separate and distinct entity.

Spontaneous remissions were frequent, and results of medical and surgical treatment were particularly difficult to evaluate. Thus far no medical therapy, including administration of acetylsalicylic acid (aspirin), corticoid preparations, diethylstilbestrol, vitamin D, sodium cacodylate, gold, and antihistaminics, has proved to be consistently effective. Synovectomy appeared to be efficacious in some patients with severely affected knee joints, but even this form of treatment was not completely successful.

Chondrosarcoma, a Surgical and Pathological Problem: Review of 212 Cases. D. C. Dahlin and E. D. Henderson. J. Bone & Joint Surg. 38-A:1025-1038 (Oct.) 1956 [Boston].

One hundred thirty-eight male and 74 female patients between the ages of 9 and 79 years with chondrosarcoma of the trunk and extremities were operated on at the Mayo Clinic between 1905 and 1955. The tumors were found in the trunk and the upper ends of the femurs and humeri in 178 (84%) of the 212 patients, and only four tumors were found in the hands and feet. Five patients died in the postoperative period. Of the remaining 207 patients, 122 were considered to have had inadequate surgical treatment and 85 were considered to have had adequate surgical treatment. There were recurrences after the original surgical procedures in 154 patients. In 139 of these, the longest interval between two consecutive appearances of the tumor was less than 5 years; in 14 the longest such interval varied between 5 and 10 years; and in only 1 was the interval more than 10 years. Consequently a 10-year interval without further appearance of the tumor is necessary to establish a cure. It is important that this interval be counted from the last surgical attack on the tumor and not from the first appearance of symptoms. Nine of the 122 patients in the inadequately treated group could not be traced, and 4 others had the last surgical treatment within the last 10 years. Four (3.7%) of the remaining 109 patients have gone more than 10 years without recurrence and are considered to be cured; 80 are dead as a result of the disease; and an additional 25 have had massive recurrence and are also considered therapeutic failures. Fourteen of the 85 patients in the adequately treated group could not be traced, and an additional 37 had received their surgical treatment within the last 10 years. Fourteen of the remaining 34 patients who are eligible for determination of a 10-year survival are alive and well; thus adequate therapy was successful in 41% of the patients traced.

Nuclear pleomorphism, hyperchromatism, and increased number of multinucleated cells were the important features indicative of greater cytological activity, and these features were used in grading the tumors on the basis of their cytological appearance. Four patients had "borderline" tumors according to Lichtenstein and Jaffe's histological criteria, 116 patients had grade 1 tumors, 79 had grade 2 tumors, and 13 had grade 3 tumors. The grades showed some correlation with prognosis. Increased cellular activity sufficient to change the numerical grade was observed in 13 of the recurrent tumors. In eight of these, the periphery of the lobules of the recurred lesions showed a spindling of the tumor cells that occasionally resulted in areas of frank fibrosarcoma. Zones of osteogenic sarcoma were observed in two recurrent tumors. The histological changes in these 13 cases were accompanied by a clinical course that included the development of distant metastasis in several instances. The grade of the malignant growth was higher than grade 1 in only 2 of the 18 patients in whom the results of surgical treatment were considered successful after long-term follow-up. The grade of the malignant growth was higher than grade 1 in 56 of the 125 patients in whom the results of treatment were unsuccessful. Metastasis occurred in 33 patients; 14 of the metastasizing tumors were grade 1, 14 were grade 2, and 5 were grade 3. Implantation of the chondrosarcomas was the usual cause of recurrence in the patients treated inadequately. In other patients implantation occurred in biopsy or other incisions. Fifty-eight patients received roentgen irradiation, and 15 of these seemed to derive definite benefit in that the tumors regressed in size and the symptoms were somewhat relieved, although the ultimate course of the disease was not altered.

Chondrosarcoma is a neoplasm of slow growth that usually causes the death of the patient by local enlargement but that may metastasize through the blood stream or the lymphatic system. It is important to differentiate it from the nonmalignant chondromatous variants. Microscopic examination of biopsy material permits prediction of malignant course. Local control of the tumor by adequate treatment is the chief problem in therapy. Recurrence of the tumor in the proximal part of the extremity or in the trunk represents an irrevocable failure of treatment in most patients. The ease with which chondrosarcoma implants locally in surgical wounds, including biopsy wounds, constitutes a major problem in management. Osteogenic sarcoma with a prominent chondroid component should not be grouped with chondrosarcoma.

Fatigue Fissure (March Fracture) of the Tibia. H. van der Houwen Nederl. tijdschr. geneesk. 100:2521-2524 (Sept. 1) 1956 (In Dutch) [Haarlem, Netherlands].

The author observed six patients with occult fractures of the tibia in the course of 18 months in a military hospital. Three young men had fatigue fractures of both tibias. One complained of pain in the left tibia about a handbreadth above the ankle. He felt some pain on pressure, but the pain was most severe when he walked. He did not recall any injury, but he had done much walking. Roentgenoscopy revealed no changes at this time, but six weeks later a painful thickening of the tibia could be felt and roentgenography now showed a periosteal reaction. Treatment consisted of limitation of standing and walking. Several months later pain developed also in the right tibia, and a periosteal reaction was visible a little higher up than on the left side. The histories of the two other patients were similar.

Repeated roentgenographic examinations may be necessary to demonstrate these fractures, for, whereas no change may be visible shortly after the appearance of the pain, some weeks later the periosteal reaction is quite evident. The author points out that, whereas fatigue fractures of the foot (march-foot) are a well-known defect in military personnel, it is not so well known that fatigue fractures may also develop in other bones.

Intramedullary Fixation of Long Bone Fractures. L. W. Breck. Am. Surgeon 22:1005-1013 (Oct.) 1956 [Baltimore].

Breck reviews the history of intramedullary fixation of bone fractures and describes his experiences with the method, particularly in fractures of the femur and tibia. He has employed the Hansen-Street nail for intramedullary fixation of fractures of the femur since 1949 and has obtained excellent results. Union occurs in from 95 to 100% of the cases. Early ambulation is permitted, and a cast is not used. The Lottes' nail is employed by the author exclusively for intramedullary fixation of the shaft of the tibia, because the V-nail of Küntscher was not exactly the right shape, nor was it quite strong enough. The Lottes' nail is triangular in shape and the cross section of the tibia is also roughly triangular. Union was obtained in all of the 26 patients with fractures of the tibia in which the author employed the intramedullary nail.

Intramedullary fixation is the best method of treatment also in fractures of the clavicle that require open reduction, although open reduction is not needed very often in fractures of this bone. However, when the fracture cannot be reduced at least fairly satisfactorily, or where there is going to be a marked prominence at the fracture site because of an upward projection of the distal end of the proximal fragments, open reduction usually is indicated. In the author's experience about 25% of adults with clavicular fracture require open reduction. In fractures of the forearm, intramedullary fixation has not proved definitely superior to other methods, but partially threaded round pins, Street's new square pins, or certain other intramedullary devices may be used. In the treatment of fractures of the shafts of the metacarpals and metatarsals, intramedullary fixation may sometimes be useful, but, on the whole, other methods of treatment are as good or better in these locations. Intramedullary fixation of fractures of the shaft of the humerus is not generally a satisfactory method.

Streptokinase and Streptodornase and the Prevention of Postsurgical Peritoneal Adhesions. A. Innocenzi and I. Priola. Minerva chir. 11:823-827 (Sept. 15) 1956 [Turin, Italy].

The authors studied the effect of streptokinase and streptodornase on postoperative adhesions. Experiments were conducted on 24 adult male rabbits weighing from 2 to 3.5 kg. each. Animals were divided into three groups of eight each, the first group being kept as a control. Streptococci were introduced into the peritoneum of the animals of the second group during surgical intervention. Streptococci were introduced in small doses into the peritoneum of the animals of the third group every day for 10 days. All animals were operated on under thiobarbital anesthesia. The doses used in the animals of the second group were 500,000 units of streptokinase and 125,000 units of streptodornase; for the animals of the third group the total dose was 1 million units of streptokinase and 250,000 units of streptodornase. Exploratory laparotomy was performed 15 days after the intervention. Only one animal died. Large adhesions were found, especially between the stomach and the abdominal wall, in seven animals of the first group. Thin and transparent adhesions were found in four animals of the second group. No adhesions were found in the animals of the third group. There were no cases of toxicity or irritation. The best results were obtained in animals operated on with sterilized material.

Heparin in Thrombosis and Embolism: Fifteen Years' Experience. I. O. Brennhovd. Nord. med. 56:1325-1328 (Sept. 13) 1956 (In Norwegian) [Stockholm, Sweden].

Heparin was given to 197 patients with thrombosis or embolism representing mainly postoperative complications. The drug was given intravenously in daily doses of from 250 to 450 mg. in four injections, without control of the coagulation time. The treatment was continued until the patient was up, and in some cases also as a long-term treatment with reduced dosage and one or two injections daily. A certain variation in the amount needed depends on the individual response. Heparin treatment of thrombosis and embolism was found to shorten the duration of the disorder and to result in a low mortality from the complication in the acute stage. Late complications after thrombosis or embolism treated with heparin are few and presumably depend on the localization and extent of the thrombosis when diagnosis is made. Follow-up of 165 patients showed that half the patients had no sequels of the thrombosis, 38% had an insignificant swelling of the calf, and 12% had severe sequels. Hemorrhagic complications in heparin treatment are believed to be readily met with protamine sulfate. Because of the awkward form of administration, heparin is not an ideal agent for long-term treatment. It seems to be the ideal treatment in the acute phase of thromboembolism and the only treatment in cases where the patient can be mobilized in bed early and is not subjected to long confinement to bed. According to Jorpes, six days' ineffective treatment with heparin points to possible complications other than thrombosis or embolism.

NEUROLOGY & PSYCHIATRY

Meninges and Choroid Plexuses in Acute Anterior Poliomyelitis. G. C. Angela and G. Giuliani. Minerva med. 47:657-661 (Sept. 15) 1956 (*In Italian*) [Turin, Italy].

The authors studied the meninges and the choroid plexuses obtained from the autopsy of 15 patients who died of acute anterior poliomyelitis. Meningeal alterations along the neuraxes and the locations of these alterations in relation to the nervous tissue underneath were searched for. The choroid plexuses of the fourth and lateral ventricles were systematically examined. A marked hyperemia of the meningeal vessels could be seen macroscopically. Macroscopic examination did not show any marked alterations in the choroid plexuses; there was, however, some evidence of passive hyperemia and of some edema. Microscopic examination showed marked changes in the structure of the meninges. The nervous tissue underneath was often altered, but at times it was intact. There were no important changes in the ependyma of the brain, of the ventricles, and of the central canal of the spinal cord. The authors think that in cases of nonparalytic acute anterior poliomyelitis there is a meningeal reaction that is similar histologically to a serous reaction.

Paralysis of the Bladder in Poliomyelitis. F. Di Nola and G. C. Angela. Minerva med. 47:655-657 (Sept. 15) 1956 (In Italian) [Turin, Italy].

The authors found paralysis of the bladder in 5.9% of the patients with poliomyelitis treated in their hospital from 1951 to 1953. Remission ensued in from 10 to 15 days. Results are given of a study made on more than 20 monkeys injected with poliomyelitis virus of the Brunhilde strain. Paralysis followed in from six to nine days. Paralysis of the bladder was found in 20% of the animals. The parasympathetic cells of the excretory sacral nuclei appeared intact. The complete recovery of the excretory function in all cases indicates that vesical paralysis must be the result of functional and not of anatomic lesions.

Intra-arterial Growth Hormone Treatment in Chronic Poliomyelitis: Results in 12 Cases. E. Henríquez Inclán. Medicina 36:359-374 (Aug. 10) 1956 (In Spanish) [Mexico, D. F., Mexico].

Satisfactory results from intra-arterial injections of growth hormone are reported in 12 patients between the ages of 2 and 15 years with chronic sequels of poliomyelitis. Sequels had lasted between 6 months and 15 years. Medical and surgical treatment failed. Four patients had the treatment only in one leg and eight patients had it in both legs. The growth hormone was given in doses that varied between 1 and 2 cc. in 1.5 cc. of saline solution for each injection. The injections were given once a week to a total of from three to eight injections for each leg treated. The patients were observed for one and a half to four months. It was observed that the necessary period for appearance of favorable results of the treatment of the leg depends on the chronicity and the degree of paralysis. When muscular movement of the legs is present, even if moderate before the treatment, the movements increase from the very first injections, and they continue to improve as the treatment progresses. The general reaction of the leg to the treatment is manifested by improvement (or appearance) of muscular movement, improvement of the muscular tonicity and of the local temperature of the skin, and appearance or increase of patellar, plantar, and achilles reflexes. The muscles increase in thickness and the leg in size during a period that varies between two and four weeks. The muscular reaction to faradic and galvanic currents and the chronaxia of the muscle increase. The results are marked for the leg in which the injections are given and moderate for the leg in which they are not. A histological study was made of a portion of a gemellus muscle before start of the treatment, and on the 20th day of its course there was a marked increase of the number of capillaries and improvement of the muscular tissue toward a normal aspect. The treatment is harmless. This is a preliminary report.

Effect of Unabsorbed Radiographic Contrast Media on the Central Nervous System. F. L. Davies. Lancet 2:747-748 (Oct. 13) 1956 [London, England].

A follow-up of 119 patients who had undergone 125 myelograms for various diseases of the spinal cord from 1 to 15 years earlier are reported. Myodil was used in 124 cases and Lipiodol in one. The length of follow-up was from 1 to 15 years. The average amount of medium injected was 5 ml.; not less than 3 ml. or more than 6 ml. was ever used. An attempt at removal of the medium had been made in only six cases, but all the patients showed residual contrast medium in the subarachnoid space: in one it was present within the cranial cavity only, in 68 in the spinal theca only, and in 50 in both situations. Seventy patients manifested abnormal reactions to the injection of the contrast medium, in 56 they were noted immediately after the injection or within a few hours, and in 14 the symptoms had persisted or had developed later and were found when the patients were examined a year or more after the myelography. The immediate reactions were severe in 47 and mild in 9. Headache, alone or with neck stiffness, nausea, vomiting, and giddiness, was common. Severe pain in the spine, usually lumbar but occasionally cervical, was also common. The symptoms lasted from a few hours to 14 days. Meningism, cranial-nerve palsy, and nystagmus followed cisternal myelography. The symptoms of meningism lasted three days, the cranial nerve palsy three weeks, and the nystagmus two weeks.

While the true incidence of persistent symptoms due to unabsorbed contrast medium is difficult to assess, they were significant in 14 patients in this series. Laminectomy was performed on five patients a year or more after myelography. In four patients it was the second operation, and in each case the arachnoid was found to be thickened and lined by a tough sticky white exudate. The nerve roots were adherent to the exudate. Three patients who had undergone myelography from one to four years previously died from causes other than their original disease. In all three the pia-arachnoid showed changes similar to those found in the surgical cases. The proportion of severe symptoms cannot be ignored and shows that there is need for restraint in employing this procedure. The contrast medium should be removed, if possible, after myelograhpy.

The Emotional Factor and the Epileptic Attack. I. M. Allen. New Zealand M. J. 55:297-308 (Aug.) 1956 [Wellington, New Zealand].

The clinical material on which this study is based consists of (1) the 182 patients with epileptic symptoms most recently examined in detail; (2) the first 622 patients with epileptic symptoms examined from 23 years ago, for purposes of comparison and control of the interpretation of the clinical data; and (3) the case material on which studies were made on reflex epilepsy, myoclonus epilepsy, epileptic automatism, temporal lobe discharges, small epileptic attacks, forced thinking as part of the epileptic attack, and other aspects of epilepsy. It was found that the emotional factor has an effect in aggravating the frequency and severity of epileptic attacks in over one-quarter of the cases. Facts show that the association of the emotional factor and the epileptic discharge is in most cases of general rather than local significance so far as the original site of discharge is concerned, that an association based upon the production of biochemical changes, effects on the blood pressure, or conditioning at the level of the cerebral cortex is uncommon; that an association based on the origin of the discharge in the temporal lobe is also very uncommon and even rare; that the association can usually be recognized by study of all aspects of the history and variations found on examination; and that treatment directed to it may in favorable cases eliminate one of the most potent factors precipitating epileptic symptoms in the individual who is prone to them

PEDIATRICS

Treatment of Chorea Minor with Prednisone and with Prednisone Associated with Chlorpromazine. I. Lanza and R. Morbidelli Minerva pediat. 8:1131-1134 (Sept. 22) 1956 (In Italian) [Turin, Italy].

The authors treated 10 patients with chorea minor with prednisone and with prednisone combined with chlorpromazine. Patients were divided into two groups of five patients each Rheumatic etiology was presumed in the patients of the first group. Prednisone alone or combined with penicillin or methylandrostenediol was given. Remission of the symptoms followed in a relatively short time. Starting dose was 1.5 to 2 mg. per day for each kilogram of body weight, continued for from two to three days. Maintenance dose was from 0.5 to 1.5 mg. per day for each kilogram of body weight, continued for at least 15 days.

Patients of the second group received prednisone combined with chlorpromazine. Two milligrams of the combination per each kilogram of body weight per day were given. Three patients in whom the origin of the disease was rheumatic improved markedly. Two patients in whom the etiology of the disease was unknown took a longer time for recovery: in one remission of the symptoms followed after 12 days, and the other improved very slowly within a month. No untoward side-effects were noticed.

The Changing Pattern of Rheumatic Heart Disease: The Experience in New York City Department of Health Cardiac Consultation Clinics, 1943 to 1953. L. Kuskin and M. Siegel. J. Pediat. 49:574-582 (Nov.) 1956 [St. Louis].

An analysis was made of the clinical diagnosis carried out in 65,044 children who were examined at the Cardiac Consultation Service Clinics of the New York City Health Department between 1943 and 1953, in order to determine whether there has been a change in the relative frequency of organic heart disease after rheumatic fever. The relative frequency of detectable heart disease occurring in children with a history of rheumatic fever who were referred to the consultation service from child health stations, elementary and high schools, mercantile working paper clinics, private physicians, and, on occasion, hospital clinics and community welfare agencies, decreased from about 60% in 1943 to about 30% in 1948. The 30% frequency level has been maintained since 1948.

These findings are related in time to the widespread use of antibiotics and are consistent with the decrease in prevalence of rheumatic heart disease reported from other source material by various investigators. They represent supportive data on the changing pattern of rheumatic heart disease.

Salicylate Intoxication. H. D. Riley, Jr. and L. Worley. Pediatrics 18:578-594 (Oct.) 1956 [Springfield, Ill.].

Salicylate intoxication occurred in 42 children between the ages of less than 1 and 6 years at the Vanderbilt University Hospital in Nashville, Tenn., between 1945 and 1955. Poisoning was caused by acetylsalicylic acid (aspirin) in 41 patients and by sodium salicylate in one. It occurred as a complication of therapy for some concomitant disease in 29, 6 of whom had rheumatic fever, and was the result of accidental ingestion in 13. Most of the accidental cases occurred in children between the ages of 2 and 4 years, the age of insatiable curiosity and some measure of independence. Therapeutic intoxication occurred chiefly in infants less than one year of age. Cumulative therapy intoxication is more likely to occur in infants than in older children not only because of an unawareness of the dangers and of the proper dose of acetylsalicylic acid but also because of the decreased renal excretion of salicylates due to renal immaturity and prerenal azotemia caused by dehydration resulting from the disease for which the drug is given.

The response of the individual patient to the salicylate varied considerably. Even in poisoning resulting from accidental ingestion, in which the effects of an underlying disease do not have to be considered, the plasma concentration of salicylate, clinical response, degree of toxicity at a given concentration of salicylate, and time required for renal excretion varied greatly for children of the same age and size who ingested comparable amounts of salicylate. Severe intoxication at low concentrations of salicylate in the plasma was observed. Hyperventilation and vomiting were the most common clinical manifestations of salicylism, but a hemorrhagic diathesis caused by hypoprothrombinemia; hyperpyrexia; delirium or coma; circulatory collapse; and respiratory failure were occasionally observed.

Because of the unique effect of salicylates on acid-base balance, with an initial respiratory alkalosis progressing to a metabolic acidosis, treatment must be individualized, flexible, and directed by physiological principles. The increased metabolic rate, polyuria, diaphoresis, and the need for enhanced urinary volume demand that adequate amounts of fluids be provided. Until serum pH and carbon dioxide concentrations have been determined, dextrose solutions to equal full maintenance and estimated deficit requirements should be administered intravenously. If respiratory alkalosis exists, sodium chloride solution should be added to the parenterally given fluids so that salt depletion can be avoided. Convulsions should be treated by administration of oxygen; tetany can be controlled by administration of calcium gluconate or inhalations of 5% carbon dioxide. If and when acidemia occurs, alkalinizing salts should be administererd. Shock should be combatted with whole blood, albumin, and plasma transfusions. Barbiturates should not be routinely used in an effort to decrease the hyperventilation, but might be used as a last resort in certain cases. A clinical trial with exchange transfusions is warranted in selected cases of salicylate poisoning.

Five patients died, and it seemed that the combination of the disease, for which the acetylsalicylic acid was given, with the salicylate poisoning was responsible for the deaths. The important role of acetylsalicylic acid ingestion as a cause of death is reemphasized and a plea is made for better education and attention to the potential dangers of salicylates.

Congenital Endocardial Fibro-Elastosis: II. A Clinical and Pathological Investigation of Those Cases Without Associated Cardiac Malformations Including Report of Two Familial Instances. J. Kelly and D. H. Andersen. Pediatrics 18:539-555 (Oct.) 1956 [Springfield, Ill.].

Seventeen cases of congenital endocardial fibroelastosis without associated malformations of the heart or great vessels and without myocarditis or other known cause for the cardiac changes were selected from the autopsy protocols of 237 children aged less than 13 years with congenital heart disease who died at the Babies Hospital in New York City in the course of a 20-year period ending June, 1955. Seventy-nine similar cases have been collected from the literature. Two instances of familial incidence were present in 3 of the 17 cases. There were several instances of the disease in one or more of multiple births, and three instances of two affected siblings among the 79 cases.

Evidence is presented that the 96 cases of congenital endocardial fibroelastosis without associated cardiac malformations represent a disease entity with the following characteristic features: 1. The disease is familial. 2. Nonspecific symptoms begin in the first six months of life in most patients; they consist of failure to gain weight and of cough, over a few days or weeks. A sudden attack of labored breathing and tachycardia with vomiting or abdominal pain may lead to death within one or two days or to recovery followed by repetition of similar attacks. Death within a day of onset of an attack occurs in 50% of the patients. 3. The heart is grossly enlarged, mainly because of dilatation and hypertrophy of the left ventricle. 4. The endocardial fibroelastosis increases with age and is most pronounced in the left ventricle. 5. Noncardiac malformations are rarely present. 6. Bradycardia before birth and congenital heart block occurred in 2 of the 17 patients.

The reported data are compatible with the hypothesis that the disease represents a congenital familial metabolic defect leading primarily to weakness of the myocardium and secondarily to fibrosis of the endocardium.

Atrial Flutter in a Newborn Infant. J. A. Segal. Connecticut M. J. 20:700-702 (Sept.) 1956 [New Haven, Conn.].

The author reports an instance of atrial flutter with 2:1 block in a newborn baby. The rapid regular heart rate was discovered three days before birth at a routine prenatal checkup. Examination of the baby shortly after birth revealed a heart rate of about 200 per minute and some slight cyanosis of the extremities. The next day there was evidence of early heart failure. An electrocardiogram taken 20 hours after birth revealed atrial flutter with 2:1 block. An x-ray on the same day showed cardiac enlargement. Digitalization converted the atrial flutter into normal sinus rhythm within 24 hours. An x-ray taken three days later showed some shrinking of the cardiac silhouette. The baby was discharged from the hospital in good condition on the 16th day.

Progeria: Report of a Case with Cephalometric Roentgenograms and Abnormally High Concentrations of Lipoproteins in the Serum. *I. M. Rosenthal, I. P. Bronstein, F. D. Dallenbach and others. Pediatrics* 18:565-577 (Oct.) 1956 [Springfield, Ill.].

The authors describe a typical case of progeria (Hutchinson-Gilford syndrome) in a girl, in whom the diagnosis was made at the age of 20 months. The patient was followed up to the time of her death, which occurred at the age of 11 years as the result of an accident at school. Analysis of cephalometric roentgenograms of the patient revealed that the characteristic facial expression of progeria resulted from pronounced retardation of facial growth in the presence of relatively normal growth of the neurocranium and was therefore not the result of premature aging. Atherosclerosis was revealed by autopsy. Concentrations of lipoproteins in the serum were determined by analytic ultracentrifugation during life and were found to be abnormally high, suggesting a metabolic error rather than premature aging of the arteries as the cause of the atherosclerosis. Psychological studies showed the patient to be of normal intelligence with no evidence of senilism. Analysis of these data leads to the conclusion that premature aging does not occur in progeria.

DERMATOLOGY

Cutaneous Leishmaniasis: A Report of 10 Cases. P. H. Langsjoen. Ann. Int. Med. 45:623-639 (Oct.) 1956 [Lancaster, Pa.].

The author reports observations on 10 American soldiers who had contracted cutaneous leishmaniasis in the area near Camp Pina in the Panama Canal Zone. This disease is generally believed to be transmitted by the bite of an infected sandfly. The area in which these soldiers were operating was heavily infested with the phlebotomus fly. There was evidence that all patients were infected while on jungle maneuvers, probably at night, while sleeping, and during the dry season. The clinical features of a classic case—the oval, painless, indolent ulcer with the raised dull red border, the necrotic base, and the beadlike subcutaneous nodules—are almost diagnostic. The ulcer expands by concentric zones of parasitic expansion just under the epidermis among the dermal papillae. The raised red border represents this expanding zone of active inflammation. It is the locus of active disease and the place from which the best material for diagnostic purposes can be obtained. Cold compresses were applied initially until the crusts and purulent material were cleaned up. Then the area was blocked with procaine, and the undersurfaces of the raised borders were scraped with a small curet. The material obtained was then smeared on a slide like an ordinary blood smear and stained with Wright's stain. The Leishmania organism is small, measuring from 2 to 5 μ in the longest diameter; it can be seen only under oil immersion. It is oval in shape and has well-defined cell borders, light blue cytoplasm, a large, relatively pale trophonucleus at one end of the cell, and a dark, rod-shaped blepharoblast. These organisms may be seen either singly, in groups, or within the structure of large macrophages. The visualization of the organism is diagnostic.

All patients were treated with intramuscular injections of the antimony preparation stibophen (fuadin), which produced cure in from 15 to 28 days, but four patients experienced recurrences and required a second course of stibophen therapy. Electrocardiographic changes indicative of antimonial intoxication were observed in all patients. Arthralgia developed in four patients during the first course of treatment and in all patients requiring a second course. All toxic changes were reversible. Stibophen (fuadin) is an effective and relatively safe form of treatment in otherwise healthy young white males with leishmaniasis, but the therapy is quite prolonged.

Localized Cutaneous Histoplasmosis. W. S. C. Symmers. Brit. M. J. 2:790-792 (Oct. 6) 1956 [London, England].

Solitary localized histoplasmic granulomas of the skin were found and confirmed by isolating Histoplasma capsulatum from the skin lesions of two patients, a 28-year-old Nigerian man and a 23-year-old Nigerian woman who were living in England at the time the diagnosis was made. The skin lesion was on one cheek in the man and over the lower end of the sternum in the woman. The organisms in the granulomas were of the large cell type, which had been described as H. duboisii; their cultural characteristics were typical of H. capsulatum. The infection was contracted in West Africa in each patient.

Lupus Erythematosus Treated with Mepacrine: Results of Treatment Together with Report of Cases with Recurrence on Longer Observation Period. J. P. Nielsen and J. V. Christiansen. Ugesk. læger 118:1035-1045 (Sept. 6) 1956 (In Danish) [Copenhagen, Denmark].

In 1953-1954, 97 cases of lupus erythematosus (81 of discoid type, 16 of erythematous type) were treated with mepacrine, the total dose being between 1.6 and 49.8 gm. and the average dose, 18 gm. In the first group there were excellent results in 22 patients, improvement in 34, and no or doubtful results in 25; in the second group excellent results were seen in 9 patients, improvement in 5, and no or doubtful results in 2. Fully half the patients were hospitalized during part of the treatment. No difference was demonstrable between the results in the hospitalized and the ambulant groups. Sex and duration of the disease seem to be unimportant, but extensive involvement appears to give a somewhat poorer result. Most surprising was the better prognosis for patients over 60. The etiology of lupus erythematosus is unknown. Side-effects in the form of dermatitis occurred in 5 patients, 16 had dyspepsia, and in 8 there were disturbances in sweating. Observation for about a year after the termination of treatment showed aggravation in about 80% of the patients who originally responded to the treatment. No recurrence was found after the 12th month, but only five patients were observed for over a year. The large number of recurrences within a year indicate that the treatment is symptomatic and not curative. Excellent results have been reported after chloroquine treatment of lupus erythematosus. The substance does not cause yellow coloration of the skin and causes fewer side-effects than mepacrine. Interest centers about the extent to which chloroquine in low doses can reduce the tendency to recurrence.

OTOLARYNGOLOGY

Otitic Meningitis: A Review of Cases in an Attempt to Evaluate the Results of Treatment. J. B. McBean. A. M. A. Arch. Otolaryng. 64:253-257 (Oct.) 1956 [Chicago].

Data on a group of 15 patients who had meningitis associated with acute or chronic otitis media are presented. The patients were observed at the Mayo Clinic during the 10 years from 1946 through 1955. Five of the six deaths occurred in patients with acute otitis media, and the sixth occurred in a patient in whom it was not determined whether the otitis was acute or chronic. Five of the six deaths occurred in patients in whom Diplococcus pneumoniae was identified in the spinal fluid; in the sixth, no organism was identified. All the patients who had meningitis with chronic otitis media received appropriate otologic surgical treatment and adequate antibiotic and chemotherapy, and all recovered. It seems probable that, in the patients who died, the diagnosis of otitis media or meningitis was not made early enough or that adequate antibiotic therapy or chemotherapy had not been given prior to hospital admission. Patients with acute otitis media and meningitis who recovered all received relatively large doses of antibiotic agents and sulfonamide. Although meningitis is a relatively rare complication of otitis media, the 40% mortality (six deaths in 15 patients) indicates that it is extremely serious. Fulminating meningitis might be prevented by early diagnosis and vigorous treatment of acute otitis media. To facilitate early diagnosis of meningitis the author recommends that spinal puncture be performed in patients with unexplained fever, convulsions, and headache; this would result in earlier institution of adequate therapy.

Improvement of Hearing in Otosclerosis by Means of Stapes-Mobilization Operation: Report of Results and Experiences. D. Myers and B. J. Ronis. *A. M. A. Arch. Otolaryng.* 64:307-323 (Oct.) 1956 [Chicago].

The authors describe experiences with Rosen's stapes-mobilization operation, which were obtained in 161 operations on 139 patients in a period of 18 months. Sixty-five (47%) of the patients were improved, while 74 (53%) were not improved. Two patients with failure underwent a successful fenestration. No surgical difficulties were encountered because of the previous stapes operation. While a degree of proficiency can be acquired with practice on cadavers, the feel of mobilizing the stapes can be obtained only on the living patient with otosclerosis. Only rarely will the cadaver specimen give the opportunity of mobilizing a fixed stapes. At first the results may be discouraging, and, due to lack of experience, complete mobilization may not be obtained, the crura may be fractured, or the incus may be disarticulated. With regard to the selection of patients the authors say that at the present time the successful candidate cannot be predicted preoperatively. The degree of stapes fixation cannot be predicted by the preoperative audiologic survey. There has been no correlation in this series between the degree of fixation, the degree of deafness, the length of time the deafness existed, and the amount of pressure or pull needed to obtain mobilization. Patients with every degree of deafness due to otosclerosis were operated on in order to explore the possibilities of Rosen's procedure. The stapes-mobilization operation has opened a new vista in the surgical rehabilitation of the deafened patient with otosclerosis. It can restore hearing to practical or normal levels. The operation is physiologically correct, restoring the impedance-matching mechanism to normal when successful. There were no untoward complications in this series of patients.

THERAPEUTICS

Experience with a New Anticoagulant *Coumadin* (Warfarin) Sodium. D. H. Goodman. *Arizona Med.* 13:389-392 (Oct.) 1956 [Phoenix, Ariz.].

Warfarin sodium, a coumarin derivative, was given routinely to 150 patients with coronary thrombosis with myocardial infarction and to patients with other conditions requiring anticoagulant therapy, such as thrombophlebitis, phlebothrombosis, phlebitis migrans, and cerebral thrombosis. The drug can be given intravenously as well as orally. Results show that a single dose of from 50 to 75 mg. given intravenously or orally will within 24 hours induce a therapeutic hypothrombinemic response. A therapeutic hypoprothrombinemia was readily maintained by a daily dose of 10 mg. or an intermittent dose of 25 mg. at three-day intervals. Bleeding occurred in 12 patients (8%); it was manifested primarily by hematuria and was readily controlled by intravenous administration of vitamin K (Mephyton). No undesirable side-effects or toxic reactions, such as cutaneous reactions or blood dyscrasias, were observed. The contraindications to the use of warfarin are similar to those for bishydroxycoumarin (Dicumarol). Warfarin should not be given to patients with all types of purpura and other blood dyscrasias, associated with a hemorrhagic tendency; patients with liver disease; patients who recently have been subjected to surgical treatment of the central nervous system; and patients with ulcerative lesions of the gastrointestinal tract, dissecting aneurysm, renal insufficiency, and with carcinoma of the body and the tail of the pancreas associated with thromboses. Warfarin possesses properties that make it most nearly the ideal anticoagulant of all those available at present. The low cost of warfarin is a factor of particular importance in long-range ambulatory treatment. Less frequent prothrombin determinations are needed because of the smoothness of the prothrombin response and absence of cumulative effect.

Analgesic Properties of Mixtures of Chlorpromazine with Morphine and Meperidine. G. L. Jackson and D. A. Smith. Ann. Int. Med. 45:640-652 (Oct.) 1956 [Lancaster, Pa.].

Clinical observations on the enhanced effectiveness of narcotics given with chlorpromazine suggested that more complete and longer-lasting relief from pain may be expected as a result of concomitant administration of these agents. Tests were carried out on 211 patients to verify the clinical impression. It was found that, when chlorpromazine is combined with morphine, the analgesic properties of the combination are greater than those of either drug alone. The addition of chlorpromazine to 25 mg. of meperidine hydrochloride produces an analgesic response similar to that seen with 75 mg. of meperidine. Chlorpromazine administered prior to morphine increases the analgesic effectiveness of the second agent. Likewise, chlorpromazine administered prior to certain combinations of morphine and chlorpromazine appears to increase the effectiveness of the combinations.

Cobalt-Iron Therapy for Common Types of Anemia. D. C. Ausman. Journal-Lancet 76:290-294 (Oct.) 1956 [Minneapolis].

The author reports observation on 44 patients with anemia. Anemia in 10 patients, of whom 4 had arthritis, 4 carcinoma, and 2 thyroid insufficiency, responded well to cobalt-iron therapy. The comparative efficacy of iron and of cobalt-iron was studied in 18 women with iron-deficiency anemia due to menstrual blood loss or previous pregnancy. With iron alone, 12 of 18 patients improved their hematological status; 6 did not. With cobalt-iron therapy, 17 patients improved hematologically; only one did not. An additional group of nine iron-deficient anemic patients who had not received iron therapy previously were also treated effectively with cobalt-iron. Gastrointestinal conditions or dietary abnormalities were associated with anemia in seven patients. In none did iron deficiency appear to be the primary factor. In five of these patients response was poor to iron therapy but excellent to cobalt-iron, as it was in two additional patients, in whom iron alone was not used initially.

Routine use of cobalt-iron therapy offers advantages over the use of iron alone in the treatment of many common anemias seen in general practice. This is particularly true of the iron deficiency anemia occurring so often in women as a result of menstrual blood loss or pregnancy. The cobalt-iron preparation was not only more rapid and effective than oral administration of iron but was effective even in patients who failed to respond to the intravenous administration of iron. The gastrointestinal tolerance for cobalt-iron was similar to that shown for ferrous sulfate. A skin rash appeared in two patients during cobalt-iron therapy. It was not severe enough to discontinue therapy and disappeared promptly when treatment was completed.

Therapeutic Effects of Prednisone in the Treatment of Typhoid and Brucella Infections. A. Alfano and G. Amati. Riforma med. 70:1078-1081 (Sept. 22) 1956 (In Italian) [Naples, Italy].

The authors report the results obtained with prednisone in six patients with typhus, two with paratyphoid, and four with brucellosis. The ages of the patients ranged between 22 and 58 years. Treatment was started between the 6th and 25th day in patients with typhus and between the 10th and 32nd day in patients with brucellosis. Two patients with typhus had previously been treated with chloramphenicol, and one patient with brucellosis had previously been treated with aureomycin for five days. Prednisone treatment was given for from 4 to 6 days in patients with typhus and for *from 6 to* 11 days in patients with brucellosis. Patients with typhus were given 30 mg. per day, with a total dose of 90 to 110 mg., and those with acute brucellosis were given a total of 110 to 190 mg., also in doses of 30 mg. per day. The hormone was given alone to one patient with typhus and one with paratyphoid; the other patients with typhus and paratyphoid received it in combination with chloramphenicol, and patients with brucellosis received it in combination with tetracycline. Fever dropped in from 12 to 20 hours. The effect on cenesthesia was rapid and marked: euphoria ensued a few hours after the hormone had been given. Toxic symptoms and headache disappeared rapidly. The pulse and the blood pressure of patients with typhoid improved. Asthenia, profuse perspiration, and muscular pain regressed markedly in patients with brucellosis. There were no side-effects. Prednisone given in small doses has an effect superior to that of cortisone, it is less toxic, and it is particularly helpful in the therapy of infectious diseases of the septicemic type.

PHYSIOLOGY

Sex Chromatin in Oral Smears. A. D. Dixon and J. B. D. Torr. Brit. M. J. 2:799-800 (Oct. 6) 1956 [London, England].

Oral smears were taken from 98 females and 162 males between the ages of 16 months and 60 years, in an attempt to test the validity of the oral smear method as an aid in diagnosis of the chromosomal sex made on sex-chromatin findings in the nuclei of the epithelial cells from the mucous membrane of the oral cavity. Sex-chromatin was not observed in the 162 male smears examined, but in most of the 95 suitable female smears, 35 to 50% of the cells counted contained a sex-chromatin mass. Thus the chromosomal sex was determined with considerable accuracy in the persons from whom the oral smears were obtained. As experience in the examination of the smears was gained, the diagnosis of the chromosomal sex became progressively more accurate. The procedure is simple in its application and if necessary may be readily repeated.

The findings in the 260 persons confirmed the previously established well-recognized difference between the nuclei of male and female epithelial cells. The mass of sex chromatin can be positively identified only in an absolutely peripheral position in the nucleus. This probably explains why, in a proportion of cells in any smear from females, the sex chromatin is not visible. In female smears the sex chromatin was usually first seen in one of the first five cells counted. As this finding occurred with great regularity it was decided that a count of 25 cells was quite adequate for sex determination. This is of particular significance in young infants in whom it may be difficult to obtain smears in which more than 25 cells fulfilling the essential criteria can be seen. These findings may help to standardize the method and insure correct diagnosis.

Physical Activity and the Diet in Populations Differing in Serum Cholesterol. A. Keys, J. T. Anderson, M. Aresu and others. J. Clin. Invest. 35:1173-1181 (Oct.) 1956 [New York].

Data on total serum cholesterol are presented for samples of men, classified by age and physical activity, in Minnesota; Malmö, Sweden; Bologna, Naples, the island of Sardinia; and three ethnic groups in Cape Province, South Africa. Data on the cholesterol in the beta lipoprotein fraction in the serum are presented for some of these groups. Differences in physical activity do not explain the large differences in serum cholesterol found when groups with different dietary habits are compared. Within some populations there is a tendency for men in heavy manual labor to have somewhat lower serum cholesterol values than the other men in the population. Among the Bantu, who show this tendency most prominently, it was found that the men in heavy work consume diets lower in fats than the other Bantu, and there is other evidence pointing to a general tendency for the composition of the diet to be related similarly to the habitual level of physical activity. It is concluded that the habitual diet, and especially its fat content, has much more influence than the physical activity, per se, on the concentration of total cholesterol and beta lipoprotein cholesterol in the blood serum.

BOOK REVIEWS

Dermatology. By Donald M. Pillsbury, M.A., D.Sc., M.D., Professor and Director of Department of Dermatology, University of Pennsylvania School of Medicine, Philadelphia, Walter B. Shelley, M.D., Ph.D., Associate Professor of Dermatology, University of Pennsylvania School of Medicine, and Albert M. Kligman, M.D., Ph.D., Associate Professor of Dermatology, University of Pennsylvania School of Medicine. Cloth. $20. Pp. 1331, with 561 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W.C.2, England, 1956.

This new textbook by men active in basic dermatological research has a fresh, critical approach and an emphasis on fundamentals that makes it the best single volume on dermatology available to students and practitioners. It is not intended to replace the more encylopedic works for the specialist, but many of its sections should be of interest to dermatologists as well, particularly the brief, readable reviews of basic science, the objective evaluations of current therapy, and the reasonable discussion of psychocutaneous medicine. The authors have devoted about 20% of the book to reviews of the anatomy, physiology, pathology, bacteriology, mycology, parasitology, allergy, and genetics of the skin. They justify this emphasis by pointing out that the skin is usually given short shrift in preclinical teaching, leaving students and clinicians with little understanding of its normal functions and basic pathological patterns. All of these reviews have a conversational tone and a practical slant that should assure greater readership than usual for material of this type. The outline of basic patterns of pathological conditions in dermatology is particularly concise, logical, and comprehensive.

Another 10% of the book is devoted to methods of dermatological diagnosis. Included in this section are chapters on regional diagnosis, pediatric and geriatric dermatological diagnosis, and dermatology in the tropics. In addition, the characteristic distributions of several common skin diseases are described and illustrated, and the basic types of skin lesions are defined and pictured in excellent black and white photographs. The next 5% of the book deals with the general principles of dermatological therapy, including topical and systemic measures. The discussion of the use of ionizing radiation in dermatology is ultraconservative, but this is preferable in an introductory text. The remainder of the book deals with the diagnosis and therapy of individual dermatoses. The material is presented in a readable, informal manner, and definite opinions and guidance are given throughout. The discussions of cause and therapy are refreshingly critical. The authors tend to reject much traditional therapy that has not been proved by controlled study. They are perhaps too pessimistic about the treatment of acne and superficial fungus infections and too hasty in discarding ammoniated mercury as an antibacterial agent. Detailed descriptions of histopathological changes in individual dermatoses are not given, but the authors indicate those diseases in which skin biopsy is helpful or essential. All in all, this is an important new book that should have many future editions.

Venous Return. By Gerhard A. Brecher, M.D., Ph.D , Julius F. Stone, Professor of Physiology, Department of Physiology, College of Medicine, Ohio State University, Columbus. Cloth. $6.75. Pp 148, with 55 illustrations. Grune & Stratton, Inc., 381 Fourth Ave., New York 16, 99 Great Russell St., London, W.C.1, England, 1956.

This is an excellent presentation of a difficult and sometimes controversial subject. It is clear, readable, and thorough. It was not within the scope of this short monograph to survey the entire field of venous physiology. Instead, the author has confined himself in the main to analysis of the several major mechanisms' that determine venous return to the heart. Much of the information presented is recent, some of it previously unpublished and derived from the author's experiments that used high-fidelity methods of measuring venous flow. There is an historical review, two chapters on basic venous hemodynamics, and a review of various methods, old and new, of measuring blood flow. Through the use of profuse illustrations of good quality, and of a concise text, the present status of the roles of ventricular ejection, the respiratory pump, systolic ventricular attraction, the muscle pump, venomotor activity, and diastolic ventricular suction in return of blood to the heart is brought into sharp focus. There is particular attention given to the author's investigations on the diastolic ventricular sucking effect. Of special interest to thoracic surgeons are a review of the effect of artificial respiration on venous return, a short chapter on venous hemodynamics in the presence of lesions of the cardiac valve, and a chapter on venous return during cardiac surgery. A helpful feature of the book is the inclusion of a brief summarizing statement of each major topic. The bibliography is complete and the index good. As stated in the foreword, written by Dr. Wiggers, "This monograph is the only current one that gives a comprehensive analysis of the determinant of venous return and its adaptation to cardiac output based on experimental measurement of venous flow. It should be welcomed alike by laboratory investigators and clinicians who must at all times be alert to avoid procedures that interfere with natural factors favoring venous return"

Peripheral Vascular Disorders. Edited by Peter Martin, V.R D, M Chir, F.R.C.S., Surgeon to Chelmsford and Billerecay Hospitals, Essex, England, R. Beverley Lynn, M.D., F.R.C S., Assistant Professor of Surgery and Markle Scholar, Medical College, University of Saskatchewan, Saskatoon, J. Henry Dible, M.B., LL.D., F.R.C.P., Director of Pathology, Postgraduate Medical School, London, and Ian Aird, Ch.M., F.R.C.S , Professor of Surgery, University of London, London. Cloth. $20. Pp. 847, with 450 illustrations. E. & S. Livingstone, Ltd., 16 and 17 Teviot Pl , Edinburgh 1, Scotland, *Williams & Wilkins Company, Mount Royal and Guilford Aves*, Baltimore 2, 1956.

This comprehensive and lucidly written volume is the combined effort of nine contributors, five of whom either are surgeons or are working in related fields. Three are research workers in the basic sciences, and one is a radiologist. The plan used in writing this book is a reflection of the interests of the authors, with the medical point of view conspicuously absent. The first portion of the book is devoted to the basic anatomy and physiology of the peripheral vessels and the laboratory and clinical methods of studying the circulation. The role of the sympathetic nervous system and its innervation of the vascular tree are stressed. Numerous diagrams and photomicrographs help to elucidate the text. The section also contains an excellent chapter on the radiology of peripheral vascular disorders. Included are descriptions of the results of soft-tissue x-ray technique, arteriography, and venography. The various pathological alterations are profusely illustrated by instructive photographs of high quality.

The remainder of the volume deals with the pathology, clinical manifestations, and treatment of diseases of the arterial, venous, and lymphatic systems. A good portion of this section is devoted to pathological alterations, particularly those of atherosclerosis and thromboangiitis obliterans. Gross changes in the arterial tree are graphically depicted through the use of roentgenograms of amputated limbs in which the arteries and their branches have been outlined by a radiopaque medium Numerous photomicrographs are used to show the different microscopic changes in the lumen of the vessels. With regard to treatment, throughout the text emphasis is placed on surgical therapy. The indications and contraindications for sympathectomy are presented in much detail. The last chapter is devoted entirely to descriptions of the various operations used in peripheral vascular disorders. Included are relatively new methods, such as the use of venous and arterial transplants, as well as the older conventional techniques. The various steps are presented in sufficient detail to be of value to the surgeon.

Even superficial perusal of the text reveals evidences of inadequate proofreading and editing. There are numerous mistakes in grammar and typographical errors, and references to subject matter elsewhere in the volume or to figures are not always accurate. Different methods of presenting the extensive bibliographies are used in the various chapters. In some instances photographs are duplicated; for example, figure 359 on page 652 is also presented as figure 385 on page 709. Figures 313 and 314 appear to be the same except that one is in color and the other, in black and white. This volume should be of real value to the specialist in peripheral vascular disorders, particularly the vascular surgeon. Much of the detailed subject matter, however, is not presented in a manner that permits ready clinical applicability to the problems of the general practitioner.

QUERIES AND MINOR NOTES

PALLOR ON EXPOSURE TO COLD

To the Editor:—*A 30-year-old man has severe erythralgia of the hands, face, and feet on exposure to temperatures below 50 F. He is in good health and has no history of previous frostbite. Is there any effective treatment or prophylactic measure?* *Charles A. Lichty, M.D., Shelbina, Miss.*

Answer.—The use of the designation "erythralgia" is somewhat confusing, but it is presumed that it is used to designate pallor on exposure of the skin to cold. Associated with pallor or following the pallor there may be varying degrees of cyanosis and rubor. The diagnosis, therefore, may be Raynaud's syndrome. This is quite commonly associated with scleroderma, and careful search should be made for scleroderma, although there is no satisfactory treatment for this condition. The treatment for Raynaud's syndrome is purely symptomatic and, in many instances, unsatisfactory. Glyceryl trinitrate (nitroglycerin) ointment applied to the fingers is sometimes helpful. One of the ganglionic blocking agents commonly used in the treatment of hypertension, such as methenamine (hexamethylenamine), may be beneficial. Sympathectomy, which causes symptomatic denervation of the skin of the face and hands, is helpful in preventing episodes of discoloration on exposure to cold in approximately one-half to two-thirds of patients who are operated on. Sympathectomy of the lower extremities is almost uniformly curative in preventing episodes of discoloration of the feet on exposure to cold.

ADRENALECTOMY FOR CANCER

To the Editor:—*Has there ever been a reported case of cancer cured by adrenalectomy after other methods have failed? Since cancer patients who have undergone bilateral adrenalectomy should receive substitution therapy, what preparation is the best and at what dose? What precautions should be observed in such adrenalectomized patients? How should one observe and maintain electrolyte balance? Would the use of 5% dextrose in 500 cc. of lactated Ringer's solution be contraindicated? How long do such cancer patients live after bilateral adrenalectomy? How do you explain the fever that occurs in such patients who had undergone adrenalectomy and who apparently show no infection?* *M.D., Philippines.*

Answer.—Cancer of the adrenal has been cured by adrenalectomy. The purpose of bilateral adrenalectomy in the patient with advanced cancer has been to control the disease and to promote a remission of its painful and systemic manifestations. Although it has been tried in other types of cancer, the successful remissions have been in the "hormone dependent" tumors of the breast and prostate. Scott and Huggins in 1945 produced a remission by this procedure in a patient with advanced carcinoma of the prostate, but since cortisone was not available they were limited in their substitution therapy. The operation has been performed by many investigators since this compound has become readily available. Hundreds of patients with advanced carcinoma of the breast and prostate have had bilateral removal of the adrenals with remission of their cancer lasting from a few months to many months. None has been reported cured.

The success of the operation depends on adequate substitution for compounds that were supplied by the adrenals and are necessary to maintain the electrolyte balance and other metabolic functions without reintroducing compounds that will promote the growth of the tumor. Exactly what the compound, or its metabolic products, will do to the metabolism of a tumor is not predictable at the present state of knowledge. In the selection of an adequate adrenal substitute, it is necessary to have both an electrolyte controlling hormone and a metabolism regulating effect. Cortisone has the advantage of having a satisfactory balance between these two functions, and, when the patient receives 50 to 75 mg. of cortisone and 4 to 5 gm. of sodium chloride a day, he can be maintained indefinitely, as long as the necessary precautions are observed.

The precautions to be observed are the same as in patients with adrenal cortical hypofunction (Addison's disease). Because the treatment of the patient with cancer requires the minimum maintenance dose of cortisone in order to be most effective, the dosage will have to be worked out for the individual patient. Consequently the resistance to stress and infection is very low and care should be taken to reduce these factors as much as possible. The patient should be instructed that the necessity of taking the cortisone is not only important to his well-being but also to his life, that if he is nauseated and unable to take it by mouth it should be taken by injection, and also that the use of mineral oil and other nonabsorbable fat-soluble compounds will carry the adrenal compounds through the intestinal tract without being adequately absorbed. The serum sodium and potassium levels should be checked at regular intervals and, as it is established that adequate replacement therapy is being given, the interval can be lengthened. The urine output volume is a good index of adequate replacement and will be of normal quantity when the patient is receiving enough cortisone to excrete potassium and will keep the serum potassium level within a normal range. The serum sodium level will drop on a low dosage of cortisone unless the sodium chloride intake is increased. A low serum sodium level and high serum potassium level indicates inadequate dosage. A high serum sodium level and low serum potassium level indicates over-replacement. It is worth while to watch also blood nonprotein nitrogen level, carbon dioxide-combining power, and serum chloride, phosphorus, and calcium levels. An elevated nonprotein nitrogen level and lowered carbon dioxide and increased chloride and phosphorus may be present if cortisone dosage is inadequate and renal output is very low for a long time, but this should be reflected first in serum sodium and potassium levels. The serum calcium level rises when the limit of the kidney to excrete it is passed. When this point is reached it is usually due to the freeing of excess calcium from the bones by the invasion and destruction by the cancer and indicates an increase in activity of the malignant cells. The use of Ringer's solution would depend entirely upon the problem that has to be treated, and if the problem required the elements in this solution it would be safe to give it. There is certainly no direct contraindication because of adrenalectomy. During the immediate postoperative period, when the cortisone dosage is usually high and urine output is large, this solution may be very helpful.

The length of time a patient lives after bilateral adrenalectomy is not limited by the operation or the substitution regimen. The cancer continues to grow but the rate of growth is much slower. It is apparently the shrinkage of each cell with release of local pressure that produces the remission of the pain and the systemic manifestations. The remission is often enough to permit many months of useful and pain-free life. Again the purpose of the operation is to withdraw a substance on which tumor growth is dependent. The tumor may regress for a time and then grow again when it finds other metabolic pathways that are not hormone-dependent.

TREATMENT OF REITER'S DISEASE

To the Editor:—*Please give an opinion concerning the treatment and prognosis of Reiter's disease.*

M.D., Pennsylvania.

Answer.—A treatment program for a patient with Reiter's disease should be planned only after giving careful consideration to the character of the disease in the individual under consideration. The disease varies widely in its manifestations from one person to another. In some instances the skin eruption is severe; exfoliating and hyperkeratotic lesions appear about the

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications and queries on postal cards cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

palms, soles, and even on the face and trunk; sometimes fever is present; and the joints may be extremely painful and swollen and the patient seriously debilitated, unable to take nourishment properly, and in need of considerable nursing care. In others, the disease is much less severe; the skin eruption may consist only of minor inflammatory changes about the palms and soles, with a few scattered lesions elsewhere on the body; conjunctivitis may appear and disappear from time to time; and the articular changes may be only slightly troublesome. In some instances the disease runs a self-limited course, all symptoms subside under the influence of careful nursing, and very little additional treatment may be required. In others, the disease progresses inexorably, producing the most intensive articular deformities accompanied by destructive changes such as may be seen in severe rheumatoid arthritis.

During acute early stages of the disease, supportive treatment should be devised to fit the particular situation in the patient under consideration. Often, complete bed rest is essential during the acute stage of the disease. If the joints are violently inflamed, splints and other supports may need to be devised in order to prevent needless pain from motion. When severe exfoliative and hyperkeratotic skin lesions are present, daily soaks or wet packs using dilute potassium permanganate solution of 1 to 10,000 aids in removing the crusts and subsequently 5% ammoniated mercury ointment may be applied to the sites of the skin lesions. For treatment of urethritis, hot sitz baths may be helpful. Irritating secretions from conjunctivitis should be washed out with saturated solutions of boric acid and mild boric acid ointment applied to the conjunctival margins. During severely painful phases of the disease, salicylates may aid in controlling the discomfort, and in some instances small doses of codeine or other narcotic may be required.

During recent years increasing experience with steroid compounds in treatment of patients with Reiter's disease has been acquired in many medical centers, and, in general, those who have employed steroid therapy have had good results. If steroids are used, prednisone or prednisolone in doses of 20 to 30 mg. daily should be given in divided doses as an initial step. Thereafter, this dose may be gradually reduced as symptoms come under control. In some instances, continued administration of steroids may be required for several months and in this event usual precautions should be taken to prevent gastric irritation by means of antacids, to prevent edema formation by reducing salt intake, and to prevent or reduce the possibility of other Cushingoid phenomena by reducing the dose as rapidly as possible in relation to the response of the patient.

STRONGYLOIDES INFESTATION

To the Editor:—*A 45-year-old woman has had Strongyloides infestation of her alimentary tract for 10 years. She has taken all possible precautions against recurrent reinfestation, and none of six immediate family members have stools positive for Strongyloides; yet she never has had a stool specimen free of viable worms or occult blood. Previous treatment included hexylresorcinol, piperazine citrate, tetrachlorides, gentian violet, and even weird concoctions advised by neighbors and fringe practitioners and by herbalists. She now has marked secondary microcytic, hypochromic anemia and feels tired and listless. I have done complete hematological studies, gastrointestinal tract series, and proctoscopic and gastroscopic examinations, which prove normal except for anemia. She has had three courses of gentian violet, enseals (2 ½-grain [30 mg.] capsules three times a day after eating) for 21 days each time. No intact enseals have been found on repeated search of stools, and yet stools continue to contain both live and dead Strongyloides. Can you suggest a better treatment?*

M.D., California.

Answer.—The adult Strongyloides worms usually are embedded in the mucosa and submucosa of the small intestine. They are small, the female measuring about 2.2 mm. Eggs, which resemble those of hookworm, hatch in the tissues or intestines, liberating the rhabditiform larvae that are found in the stool. After discharge from the body the larvae may establish a free living cycle outside the body, or, if conditions are unfavorable, the rhabditiform larvae may be converted into the infective filariform larvae. This infective form penetrates the skin of man, gets into the capillaries, takes the heart-lung route, ascends the respiratory passages to reach the esophagus, and passes down into the stomach and intestine. Some worms may migrate into the pulmonary tissue and develop there, giving rise to larvae in the sputum. The complete cycle may take place in one host, resulting in internal reinfection. In these cases the rhabditiform larvae metamorphose into filariform larvae within the intestine or on the perianal skin. These infective larvae penetrate the mucosa of the lower intestine, or the perianal skin, resulting in hyperinfection. In these cases the infection is not self-limited but continues to build up within the body in the absence of reinfection from the outside. Also the infective larvae may be ingested with uncooked vegetables and gain entrance to the body through the mucous membranes. Usually eosinophilia is present and, when absent, is a poor prognostic sign. The diagnosis is established by finding the characteristic larvae in the stool. Sometimes they are found only in material aspirated from the duodenum.

Eradication of this worm is difficult. Medicinal gentian violet is recommended but often gives unsatisfactory results. For those who do not respond to the oral therapy with gentian violet duodenal intubation is recommended. The patient should be in the hospital. The day before treatment the patient is given a liquid diet, and early next morning an enema to clear the lower part of the intestine. Then pass the duodenal tube, making sure it is in the duodenum, and inject 25 cc. of a 1% aqueous solution of gentian violet medicinal. In chronic cases of long duration this treatment will have to be repeated when the larvae in the tissues become adults. Twenty-eight days are required from the entrance of the filariform larvae through the skin to the appearance of rhabditoid larvae in the stool. In extraintestinal infections the intravenous route is recommended (25 ml. of sterile 0.5% aqueous solution of gentian violet medicinal). Diethylcarbamazine (Hetrazan) is useful in some refractory cases (2 mg. per kilogram of body weight three times daily for 10 to 20 days; total dose, 4 to 8 gm.).

PURE NEPHROSIS

To the Editor:—*A 9-month-old boy presents the picture of nephrosis. He had never been ill until he was 7 months of age, when he developed a head cold with ear, nose, and throat involvement, lasting three days, during which time his temperature reached 105 F (40.5 C) (rectal). He was treated with penicillin injections and oral medication, presumably sulfonamides. One month after his illness, the parents noted some puffiness of the eyes, followed by swelling of the feet, abdomen, hands, and face. The baby was irritable, but not feverish. There was no anuria or rusty, discolored, or grossly bloody urine. Physical examination showed only generalized edema. Blood pressure was 98/68 mm. Hg. Urine consistently showed albumin. Treatment has consisted of therapy with prednisolone, Diamox, and Thorazine. What is the prognosis for a baby who has this condition, and what future treatment is recommended?*

Charles L. Concklin, M.D., Corpus Christi, Texas.

Answer.—From the data submitted, it seems that the child has "pure nephrosis." If this is the case and no other systemic disease is involved, then the prognosis for this patient with nephrosis is similar to that for patients in older age groups: excellent for recovery, unless progressive renal failure ensues. Steroid treatment seems entirely adequate. It is not unusual to use prednisolone initially, 1 mg. per pound of body weight daily for two to four weeks until diuresis is complete and the patient has been free of proteinuria for approximately one week. This is followed by a plan of long-term steroid therapy that is satisfactory for the patient situation. Usually, the same dose of prednisolone is used three consecutive days of each week. This is continued for 9 to 12 months, as long as proteinuria is controlled. Therapeutic doses of a broad-spectrum antibiotic are used during the daily initial therapy; none are used during the period of intermittent steroid administration unless infection occurs. Diamox is not effective in the edematous stage of this disease.

TOXICITY OF XYLENE (XYLOL)

To the Editor:—*Xylene (xylol) is being used in a certain plant. What test can be depended on to determine the safe concentration of xylene in air? What are the effects of intoxicating levels and how long may workers stay in this environment? Are the effects of xylene cumulative? Should routine testing be done on workers?*

William M. Vest, M.D., Ukiah, Calif.

Answer.—Tests for the quantitative determination of xylene (xylol) levels in an industrial plant are practical but difficult. The maximum acceptable concentration of xylene is 200 ppm of air for an eight-hour work period. The vapors of xylene are so irritating to the eyes that workers usually will not work in any significantly high concentration. Xylene is the homologue of benzene and toluene but is far less toxic than benzene and perhaps of nearly the same toxicity as toluene. There may arise both acute and chronic damage. In the acute stage and in mild cases, attention should be paid to complaints of excessive fatigue, dizziness, palpitation, mental confusion, numbness in extremities, tremors, dyspnea, and anxiety. In more severe poisoning, unconsciousness may be brought about, and this, if relieved, may be followed by excitment, gastrointestinal pains, headaches, insomia, and formication; nausea and vomiting may appear. In the chronic form all acute manifestations may persist with added severity and persistence of symptoms referable to the nervous system, including stupor and paresthesia. A common complaint is that of persistent gastrointestinal disturbance. Hypotension may appear. The damage from xylene is less reflected in the cellular elements of the blood than is benzene, although low red blood cell counts may appear. Leukopenia, which is fairly characteristic of benzene poisoning, rarely occurs from the action of xylene. A relative lymphocytosis is the rule. In general, not too much is to be expected from blood cell counts in suspected xylene poisoning. At least in the past, some commercial xylene has proved to contain some benzene, which greatly adds to the prospect of injury. Recourse should be had to more adequate presentation, such as is found in Browning's "Toxicity of Industrial Organic Solvents" (Medical Research Council, Industrial Health Research Board report no. 80, ed. 2, London, Her Majesty's Stationery Office, 1953).

SEDIMENTATION RATE AFTER SPLENECTOMY

To the Editor:—*What do you consider a normal sedimentation rate for a person who has had splenectomy?*

J. M. Hesser, M.D., Benson, Ariz.

Answer.—The sedimentation rate depends on the type of tube in which the determination is carried out, and without knowing what method the inquirer uses no values can be given. The sedimentation rate appears to be dependent on several factors, i.e., the level of the total plasma proteins and the relation of the various fractions to one another; the presence of either anemia or polycythemia. A splenectomy in itself should not significantly affect the sedimentation rate. If the patient has a normal red blood cell count and if there is no underlying chronic disease, one would expect the sedimentation rate to be normal.

MUSCULAR DYSTROPHY

To the Editor:—*A 21-year-old Chinese man has atrophy of two years' duration of the muscles of both arms, thighs, and shoulders, including the pectoralis major and minor muscles, supraspinatus, infraspinatus, teres minor, and rhomboids. There is still some function of the deltoid muscles. The muscles of the forearms, hands, legs, and feet are still intact, and of normal dimensions. The upper extremity has "Popeye" configuration: no biceps muscles but full muscular forearm. What therapy would be more specific than supportive?*

Alfred O. Mazat, M.D., Singapore.

Answer.—The condition described is in all probability a scapulohumeral type of muscular dystrophy of Déjerine-Landouzy variety. Mention is not made of facial involvement, nor is any history of familial incidence given. These two phases of the disease should be investigated, since facial involvement is minor but frequent in these patients in many cases, and very minor involvement of siblings and other members of the family may be elicited with careful examination. Although isolated cases of this type of muscular dystrophy can be found, the more common type is hereditary and is transmitted as a dominant. The only diagnosis that seems to be possible, other than the above, is a chronic myositis involving both girdles, but the distribution of atrophy described in this case is most unusual for such a condition. There is no accepted form of treatment for this condition. Many drugs and preparations have been used, and the most popular at the present time is aminoacetic acid (glycine), in dosage of 10 to 20 gm. per day. This is said to retard the progression of the disease in some cases and in others has shown some beneficial effect, but never of striking character. Another treatment that has had some popularity is the administration of vitamin E in dosages between 100 and 600 mg. daily. This also is of doubtful benefit, although controversial reports have been made on the subject. Still another controversial method of treatment is that of a combination of nutritional factors such as vitamin B_{12}, folic acid, and a mixture of amino acids. The latter have been administered mostly in the form of a casein hydrolysate, although liver hydrolysates have been advocated also. All of these nutritional supplements are of doubtful specific effect.

SWADDLING AND SHORT STATURE

To the Editor:—*Asiatics, Eskimos, Laplanders, and Greeks have short stature and they swaddle their babies for the first 12 to 15 months. To what degree is swaddling, or are other factors, responsible for short stature?*

S. Partheniou, M.D., Poros, Greece.

Answer.—The practice of swaddling infants is widespread. Although frowned on by psychiatrists and pediatricians because of retarding behavioral development and possible effects on the personality of the child, it cannot be implicated in the suppression of full stature growth. Swaddling is a procedure found among both tall and short peoples. Many factors have been implicated in the development of stature, such as climate, weather, cultural practices, nutrition, and race. Of all these, only ethnic extraction and nutrition are thoroughly documented. In discussing race as a factor, it should be understood that the concept as presently used is a dynamic one. Race is no longer considered a static type, but a population concept, statistically defined and undergoing constant change in the proportions of different genetic determiners. The influence of nutrition is well documented in studies of European, Polynesian, and Mexican immigrants to the United States. Where nutrition is improved, there is a consistent increase in stature from one generation to the next, with no change in the genetic composition. This does not mean that one can increase stature indefinitely through improved diet but only that the depressing effect of poor nutrition can be negated by good diets within racial limits.

ADENOID TISSUE IN ADULTS

To the Editor:—*A 24-year-old woman had a tonsillectomy and adenoidectomy in March, 1955, after which there was persistent clear mucoid drainage from the region of the adenoids for one year. Secondary adenoidectomy has likewise failed to eliminate this drainage. Incomplete epithelization was considered as the cause. Various medicaments, including Lugol's solution, thyroid, dilute iodine in glycerine, and estrogenic nasal drops have been tried. Could you outline a regimen that might eliminate this disconcerting problem?* M.D., Ohio.

Answer.—Adults generally do not have adenoids. By adenoids is meant the diseased and hypertrophied pharyngeal tonsil, as distinguished from the faucial tonsil. It is true that many individuals do have remnants of lymphoid tissue in the area; this so-called adenoid "rest" as a rule is symptomless. If there were persistent drainage before the operation, it could have been due to one of the following conditions. 1. The remnant of pharyngeal tonsil may have had a persistent medial cleft that tended to seal over; from time to time this could open and empty itself. 2. The other condition, about which there is some disagreement, is generally termed nasopharyngeal (Thornwaldt's) bursitis. This nasopharyngeal cleft is said to spring from (*a*) notochordal contact with the nasopharyngeal mucosa, (*b*) Rathke's pouch, or (*c*)

Seessel's pocket. Such a mucosa-lined pocket can be diagnosed by careful nasopharyngoscopy, and, if present, needs to be curetted under direct inspection via the Yankauer nasopharyngoscope or by elevation of the palate by means of a Jackson soft palate retractor. Not to be forgotten are the ordinary causes of postnasal drip, which include all those irritating mucous membrane agents and conditions, so well described by Proetz (*Ann. Otol., Rhin. & Laryng.* 54:739, 1945). In addition, this case calls for ruling out of posterior cell sinusitis and nasal allergies. For therapy it is suggested that Proetz' article be consulted.

CYSTITIS

To the Editor:—*An unmarried woman, 66 years of age, has had frequency of micturition, nocturia, burning and smarting on urination, decreased bladder capacity, and pyuria for the past three years. She has been given numerous medicaments, with no benefit. Candida krusei fungus has been isolated on cultures. What would be the appropriate treatment?*

H. W. Waters Jr., M.D., Montgomery, Ala.

Answer.—Candida krusei is generally regarded as a saprophyte, and there is little or no evidence that it causes infection when found in the urinary tract. The bacteria commonly found with cystitis may be obscured on culture by the Candida (Monilia) infection. It would be advisable, therefore, to make repeated cultures as well as smears of the urine in order to determine the existence of etiological bacteria, and antibiotics should be administered according to the type of bacteria found. Involvement of the bladder with Candida often responds to lavage with a solution of methylrosaniline chloride (gentian violet) (1:1,500) or a weaker solution of acriflavine. A new drug, nystatin, has been found to be of value in treating monilial infection of the urine. It may be used both orally and as a medium for irrigation of the bladder. When used for irrigation, a solution made by dissolving one tablet of nystatin in a liter of water may be tried. Injections of Tritheon (2-acetylamino-5-nitrothiazole) also have been of value in some cases. It should be remembered that Candida infection is usually of vaginal origin, and there are many preparations that have been used locally to eliminate vaginal infections, with variable results. No mention has been made of preliminary complete urologic examination, including cystoscopy, catheterization of the ureters, and bilateral pyelography or urography. This should, of course, be done to exclude evidence of pathological conditions in the urinary tract.

INSULIN TEST AFTER VAGOTOMY

To the Editor:—*What is the insulin test as used in gastric surgery and what are the principles involved?*

M. D., New York

Answer.—The insulin test, as used in gastric surgery, depends on the discovery by Carlson and Bulatao and Wolff that a profound hypoglycemia produced by the injection of insulin stimulates the vagus centers, arousing impulses in the vagus nerves that excite the stomach to increased motility and increased gastric secretion. On the recommendations of Hollander, surgeons have made use of this physiological test to determine whether all of the vagus fibers to the stomach have been divided in the vagotomy operation. The test may be performed as follows: In the morning, with the stomach empty, the gastric content is aspirated by nasogastric suction every 10 minutes for one-half an hour to establish the control gastric secretion. The samples of gastric juice are collected separately and titrated for free hydrochloric acid with use of Töpfer's reagent. Fifteen units of regular insulin are then given intravenously and aspiration of the gastric content continued every 10 or 15 minutes for a 90-minute period. If the vagus nerves to the stomach are present, the first one or two samples of gastric juice removed may show less than the normal concentration of free hydrochloric acid but the sample collected at 20 minutes or ½ hour will usually display an increased concentration of acid, which becomes more marked at 40, 50, or 60 minutes after the administration of the insulin. The secretory response is roughly proportional to the symptoms of hypoglycemia that develop. In a patient whose vagus nerves have been completely divided, the concentration of acid in the samples of gastric juice aspirated during the hypoglycemic period does not exceed that of the control.

WESTERGREN SEDIMENTATION RATE TECHNIQUE

To the Editor:—*Do you know the method of correction of sedimentation rates for anemia when done with the Westergren technique (20 cm. column of blood)? The only correction chart I can find is that which pertains to the Wintrobe method.*

M.D., New York.

Answer.—The effect of the concentration of red blood cells on the sedimentation rate determined by the Westergren method has been studied by Ham and Curtis (*Medicine* 17:447, 1938). When the specified anticoagulant, as described below, is used in the Westergren method, the sedimentation rate is influenced relatively little by changes in the concentration of red blood cells. If other anticoagulants such as heparin or dry oxalate mixture are used, the effect of the concentration of red blood cells is large, and there is no satisfactory method for correction. The following details are suggested for the Westergren method. The Westergren "tube" is a pipet filled from the bottom. It is 300 mm. in length and 2.5 mm. in internal diameter, is graduated from 0 to 200 mm., and contains about 1 ml. The anticoagulant is an aqueous solution of 3.8 gm. of sodium citrate per 100 ml.; 0.2 ml. of the anticoagulant is added for every 0.8 ml. of whole blood, making a final concentration of 760 mg. of sodium citrate per 10 ml. of mixture and a dilution of 20% of the blood with an aqueous solution. The citrated blood is mixed and drawn up into the Westergren tube, which is then placed vertically in a stand, of special construction, that closes the bottom of the pipet by a rubber stopper and holds the tube firmly against the stopper by means of a spring. The depth of settling of the top of the red-blood-cell column is measured at the end of one hour. The author reports that the normal range for men is 1 to 3 mm. and for women, 4 to 7 mm. in one hour.

MALINGERING DURING AUDIOMETRY

To the Editor:—*What procedure is recommended for the detection of malingering when one is testing a patient for acuity of hearing with an electric audiometer?* *M.D., California.*

Answer.—The Lombard test, for total bilateral deafness, is a loudness-balance type of test, and the method of testing is generally to have the patient read out loud continuously while you increase the intensity of the sound. It will be noted that, depending on whether you are lowering or raising the intensity of the sound, the patient's voice will increase or decrease in volume. This can be done either as a unilateral or as a bilateral test. It is reliable, and the patient cannot feign this.

The repeated threshold test consists of retesting the patient at frequent intervals, that is at different times. It is difficult for the patient to remember from time to time at what frequency he was unable to hear, and in that way differences in decibel loss will vary, and one will be able to ascertain the malingering.

The swinging tone and voice test uses pure tones, instead of the masking apparatus, and is similar to the loudness-balance test.

TOXICITY OF PENTACHLOROPHENOL FUMES

To the Editor:—*An 80-year-old man with inactive, moderately advanced pulmonary tuberculosis has been painting his boat in a partially closed room with a liquid wood preserver, the base of which is pentachlorophenol. After a few hours he observed that his cough had completely abated; he remained free from cough for a number of days, after which time the cough gradually returned to its former intensity. Despite the caution on the label, he deliberately inhaled further fumes of this phenol preparation and again experienced an abatement of his cough. What is the toxic effect of continuous inhalation of fumes containing pentachlorophenol, particularly on the kidneys and liver?*

R. S. Anderson, M.D., Erie, Pa.

Answer.—It is not remarkable that pentachlorophenol appears to exert mild anesthetic properties, since many phenolic bodies do. The use described in the query may not be condoned at the present time. This substance is a known irritant for skin and mucous membranes and is believed to possess active allergenic properties. A 1% solution may provoke an acute dermatitis. When mildly heated, the vapors produce a pungent and irritating odor. Exposure to solutions is believed to be followed by skin absorption, while only scant experience with reference to inhalational effects has developed. It may be believed that, apart from local damage, the eventual severe damage may be to the circulatory system, liver, and kidneys. It is not known that any substance chemically related to pentachlorophenol is safe for use as a pulmonary sedative.

AUTHENTICATION OF VACCINATION CERTIFICATES

To the Editor:—*When there is no public health official available in the area, who is authorized to authenticate an international certificate of vaccination? Why is this second certification by a public health official necessary?*

M.D., Illinois.

Answer.—In addition to any local health officer, the certificate may be authenticated by a state health officer or an officer of the Public Health Service. The prospective traveler need not appear in person but may mail the certificate enclosing a self-addressed envelope. Health officers who do not have an official stamp to authenticate international vaccination certificates are requested to have a stamp made that includes the term "health officer" and the name and address of the health department. This stamp is required to attest to the signature of the immunizing physician, or physicians, affixed on the smallpox and cholera vaccination certificates entered in the "International Certificates of Vaccination" form. No certificate is valid without the stamp of a "health department." Public Health Service officers and medical officers of the Department of Defense will continue to use the seal of their respective service to authenticate these certificates.

Health officers of local and state health departments are required to authenticate smallpox and cholera vaccination certificates for the purpose of determining that the vaccinator is a practicing physician in the area, thereby reducing the possibility of certificates being issued by unauthorized persons. Health officers may also authenticate certificates issued by physicians in other sections of the United States if there is a means of checking the vaccinator's name, such as through reference to the American Medical Directory. Certificates issued at facilities of the Public Health Service, the Department of Defense, and designated yellow fever vaccination centers carry the stamp or seal approved for their use.

PHLEBITIS AFTER SKIING

To the Editor:—*A patient came down with acute iliofemoral thrombophlebitis after strenuous skiing. It has occurred to me that this may not be an uncommon complication among all skiers, with or without fractures. Are there statistics available of phlebitis among skiers, either in the calf or in the thigh?*

Jesse Appel, M.D., Kew Gardens, N.Y.

Answer.—A review of the literature and inquiries addressed to several other vascular surgeons as well as to numerous doctors who attend New England ski areas reveal no cases of deep phlebitis secondary to skiing. This may be due to the fact that this sport attracts healthy young participants. However, phlebitis could be caused by skiing either directly from trauma, such as fractures or muscle contusions, or indirectly from effort. The crouched skiing positions, causing angulation of the deep veins at the knee and groin in association with violent muscle contractions, could produce a tear of a valve with resultant thrombosis. Such phlebitis must be more common than is realized, and physicians may not be reporting their cases. To clarify this situation, would any physician who has observed or treated such cases kindly send a brief report to John J. Byrne, M.D., Director, Third (B. U.) Surgical Service, Boston City Hospital, 818 Harrison Ave., Boston 18.

TESTING FOR GLYCOSURIA

To the Editor:—*What is the present acceptability of the Eli Lilly product Tes-Tape as a definitive test for glycosuria?*

M.D., Arizona.

Answer.—To all intents and purposes, the product referred to gives a positive reaction only in the presence of glucose. It is highly satisfactory for determining the presence or absence of glycosuria and hence would seem to be ideal for screening purposes. However, it is considerably more sensitive than the commonly used copper reduction methods, and it has yet to be determined whether its use on a large scale will lead to an undue proportion of false-positive reactions. Possibly a minor source of confusion to diabetic patients is the fact that with this method a negative test is yellow (the original color of the paper) and a strongly positive test a dark blue or blue green, while with the copper reduction methods a blue color is negative and a yellow strongly positive. The necessity for accurate timing and the difficulty of distinguishing between different grades of glycosuria by the paper method are considered by some to be disadvantages, but these may well be offset by its great convenience.

INTRAVENOUSLY GIVEN AMINO ACID AND FAT SOLUTIONS

To the Editor:—*What is the value of intravenously given amino acid solutions? Is this form of amino acid metabolized to protein in the body? Is the difficulty in the production of solutions of fat for intravenous fusion due to the fact that proper emulsions cannot be obtained, and have ultrasonics been employed?*

M.D., Ohio.

Answer.—The intravenous administration of amino acids is important when the protein requirements of the body cannot be met by oral feeding. When bodily requirements are not supplied, the organism is forced to live on its own tissues. Amino acids for parenteral administration, available commercially as hydrolysates or mixtures of pure amino acids, can be effectively utilized in repairing or building tissue if the caloric requirements of the body are supplied concomitantly. The main difficulty in providing fat emulsions for parenteral use is the fact that the emulsions are likely to develop pyrogenic properties. Ultrasonics have been employed, but they are not effective in improving the stability of the emulsion.

TOXICITY OF INSECTICIDES

To the Editor:—*A patient held a dog while her husband sprayed it with insecticide. She inhaled some of the insecticide and shortly afterwards developed headache and symptoms suggestive of an acute brain syndrome. In spite of therapy she became comatose and died within 24 hours. Postmortem examination revealed no cause of death. The ingredients contained in the insecticide were as follows: pyrethrins, 0.51%; piperonyl butoxide, 0.512%; rotenone 0.256%; and other cube extractives, 0.472%. Is it possible that inhalation of any of these ingredients could be fatal? What are the antidotes?*

M.D., Florida.

Answer.—The ingredients in this insecticidal mixture are plant products, with the exception of the synergist, piperonyl butoxide. Botanical insecticides of the types described are capable of producing a fatal hypersensitivity reaction, but the occurrence of such a reaction is rare. The synthetic synergist has a low order of toxicity. There are no antidotes for untoward reactions to the above chemicals, and treatment, when required, is symptomatic and supportive.

CHOREA GRAVIDARUM

To the Editor:—*Please discuss the relation between pregnancy and hereditary chronic progressive chorea with mental deterioration (Huntington's chorea). I have a patient who had chorea (St. Vitus dance) and was told that the chorea was likely to recur with pregnancy.*

Robert J. Dickinson, M.D., Ridgway, Pa.

Answer.—Greenhill (Obstetrics, ed. 11, Philadelphia, W. B. Saunders Co., 1955) says: "Chorea gravidarum occurs in about one of every 3000 pregnancies and may recur in the same patient in subsequent pregnancies. It is closely associated with rheumatic infection. Its onset may be abrupt and severe, accompanied by a toxic-delirious psychosis. Of the 951 cases collected by Willson and Preece, more than 50 per cent of the women gave a history of having had chorea previously; however, there is no great danger of a recurrence during pregnancy in women who had the disease in childhood. Most authorities believe that interruption of pregnancy cures chorea; hence, they advocate therapeutic abortion if the patient's condition becomes worse in spite of conservative therapy. I believe that it is rarely necessary to interrupt pregnancy for chorea. The treatment of chorea during pregnancy is the same as in the nonpregnant state. Local anesthesia should be used for delivery whenever possible."

INTERVAL BETWEEN DPT IMMUNIZATIONS

To the Editor:—*Often through oversight DPT (diphtheria and tetanus toxoids and pertussis vaccine combined) immunization is not completed on the recommended four-to-six-week interval schedule. Is any one of the following patterns effective in producing immunity: (1) Long interval (6 to 12 months) between first and second injections with proper interval for the third; (2) proper interval between first and second injections and a long interval (6 to 12 months) between second and third; and (3) both intervals extended 6 to 12 months?* *Lawrence H. Lief, M.D., Jamesburg, N. J.*

Answer.—The generally accepted schedule of three doses of DPT injected at intervals of four to six weeks is designed to give the maximum amount of protection in the minimum amount of time. Equally high levels of immunity ultimately will be achieved after injection of DPT at greater intervals, such as those suggested in the three patterns described by the inquiring physician, the only difference being in the length of time required for the child to become immune.

HEARING HEART-LIKE SOUNDS

To the Editor:—*A physician, aged 74, complains of hearing a chest sound without the use of a stethoscope. It resembles a pericardial friction-like sound or musical whistling. It is completely synchronous with heart action and does not seem to proceed from one special part of the chest. It is most disturbing while he is in bed and when he changes position. Examination revealed that the heart is not enlarged, fluoroscopy is normal, and the only abnormal sound is a grade 2 murmur. The blood pressure is normal. Is this sound cardiac in origin, or aural? Is this common?* *M.D., Connecticut.*

Answer.—If the sound cannot be heard by an examiner who is properly trained to hear such sounds, it is altogether likely that the sound has its origin in the ear. It is not uncommon to find that a tortuous vessel impinges on some portion of the auditory apparatus and produces a noise. Most commonly this is described as a buzzing in the ears, but not infrequently it seems to the patient to have its origin elsewhere. If the patient's cardiovascular system is normal for his age, this phenomenon need cause no concern. In any event, there is little that may be done.

SEQUELA OF TRANSURETHRAL PROSTATECTOMY

To the Editor:—*A 70-year-old patient had a transurethral prostatectomy for benign hypertrophic prostatitis seven months ago. Complications included severe hemorrhage three weeks after the operation, two light hemorrhages two weeks later, and purulent infection by* Escherichia (Bacillus) coli, *with several relapsing crises for three to four months. The patient has also had lack of ejaculation until the present time. Is this a result of an obstruction of the ejaculatory ducts?*

A. A. Bernardo, M.D., Philadelphia.

Answer.—It is the rule rather than the exception that patients who have had a transurethral prostatectomy do not have external ejaculation after intercourse. The lack of ejaculation is not due to an obstruction of the ejaculatory ducts, but to the inability of the fascial muscular or mechanical action of the prostate in throwing the ejaculated seminal material out through the urethra and the external meatus at the time of crisis.

PLATELET COUNT FROM STAINED BLOOD SMEAR

To the Editor:—*How does a technician make an estimate of the platelet count from the routine stained blood smear?*

W. L. Martin, M.D., Romeo, Mich.

Answer.—The smear must be uniform and should be sufficiently thin so that the red blood cells can be counted as individual units. Use a diaphragm in the ocular or oculars, so that the field of observation is relatively restricted. This can be readily done by inserting between the two lenses of the ocular a piece of opaque material with a hole in it. Count in a number of fields the ratio between red blood cells and platelets. It is sufficient for a rough estimate to count about 200 red blood cells. Having determined this ratio, simply count the platelets in 10 or 20 additional fields without counting the red blood cells. With the ratio already known, and knowing, of course, the red blood cells, one can estimate the number of platelets with a good approximation. Experienced technicians can obtain a similar estimate by simply scanning a number of fields, as they observe other variations in the stained smear.

URINALYSIS

To the Editor:—*In routine hospital procedures the urine is collected between 5 and 7 a. m., and its examination in the laboratories may be done about 10 or 11 a. m. How exact is the report of the erythrocyte count and the leukocyte count? Are the cells dissolved during this time? Is the report that bacteria are seen of any significance in urine that has been standing in a hot environment for several hours? What kind of preservative should be added to urine at the time of collection?* *Erwin Leonhardt, Clayton, Mo.*

Answer.—It would seem that the urinalysis described is carried out about as promptly as is usual in most hospitals. Probably there is no significant loss in cells. Bacterial growth taking place in urine standing in a hot environment may be of significance if the specimen has been collected in a manner that avoids contamination; a catheterized specimen collected in a sterile container is a culture medium in which bacteria will multiply. The best preservative is refrigeration. A crystal of thymol may be used as a preservative. Textbooks suggest others that have been used, not too satisfactorily.

HOSPITAL STAFF BYLAWS

To the Editor:—*Where might I find a draft of a "model" set of bylaws governing the medical staff of a small (25 bed) rural community hospital?* *M. B. Jarman, M.D., Hot Springs, Va.*

Answer.—There are no "model" bylaws, rules, and regulations now published and up-to-date specifically for medical staffs of small rural community hospitals. In addendum 5, page 309, of "The Medical Staff in the Hospital" by Ponton (ed. 2, Chicago, Physicians' Record Company, 1953), however, "model" bylaws, rules, and regulations for medical staffs of hospitals of 50 beds or less are shown. These could be used, provided they are amended to conform to more recent recommendations regarding medical staff committees, attendance at meetings, and consultations. A guide to the wording of such amendments may be found in the "Principles for Establishing Medical Staff Bylaws, Rules and Regulations" published by the Joint Commission on Accreditation of Hospitals, 660 N. Rush St., Chicago 11. It should be emphasized that "model" bylaws should be modified to meet the individual hospital's needs.

STOMATITIS AND VAGINITIS DURING MENSTRUATION

To the Editor:—*A married woman, 28 years of age, each month at menses develops ulcerative stomatitis and glossitis and acute ulcerative vaginitis, also some dermatitis. She has visited many doctors. She gets much relief from taking vitamin B, but still develops the same symptoms. Have you any further suggestions on diagnosis and therapy?*

Lorne W. Mason, M.D., Evanston, Ill.

Answer.—There are cases in which unusual symptoms that develop just before menstruation yield to the therapy generally administered for premenstrual tension. Therefore, in addition to the use of vitamin B, which does give relief to this patient, other therapy should be added. Two popular forms of therapy are ammonium chloride, 0.6 gm. three times a day after meals for about 14 days before the expected onset of menstruation, with restriction of salt, or a 5-mg. tablet of testosterone propionate for sublingual or buccal administration daily for about 10 days before menses begin.

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The letters used to explain in which department the matter indexed appears are as follows: "E," Editorial; "C," Correspondence, "ab," abstracts, the asterisk (*) indicates an original article in THE JOURNAL.

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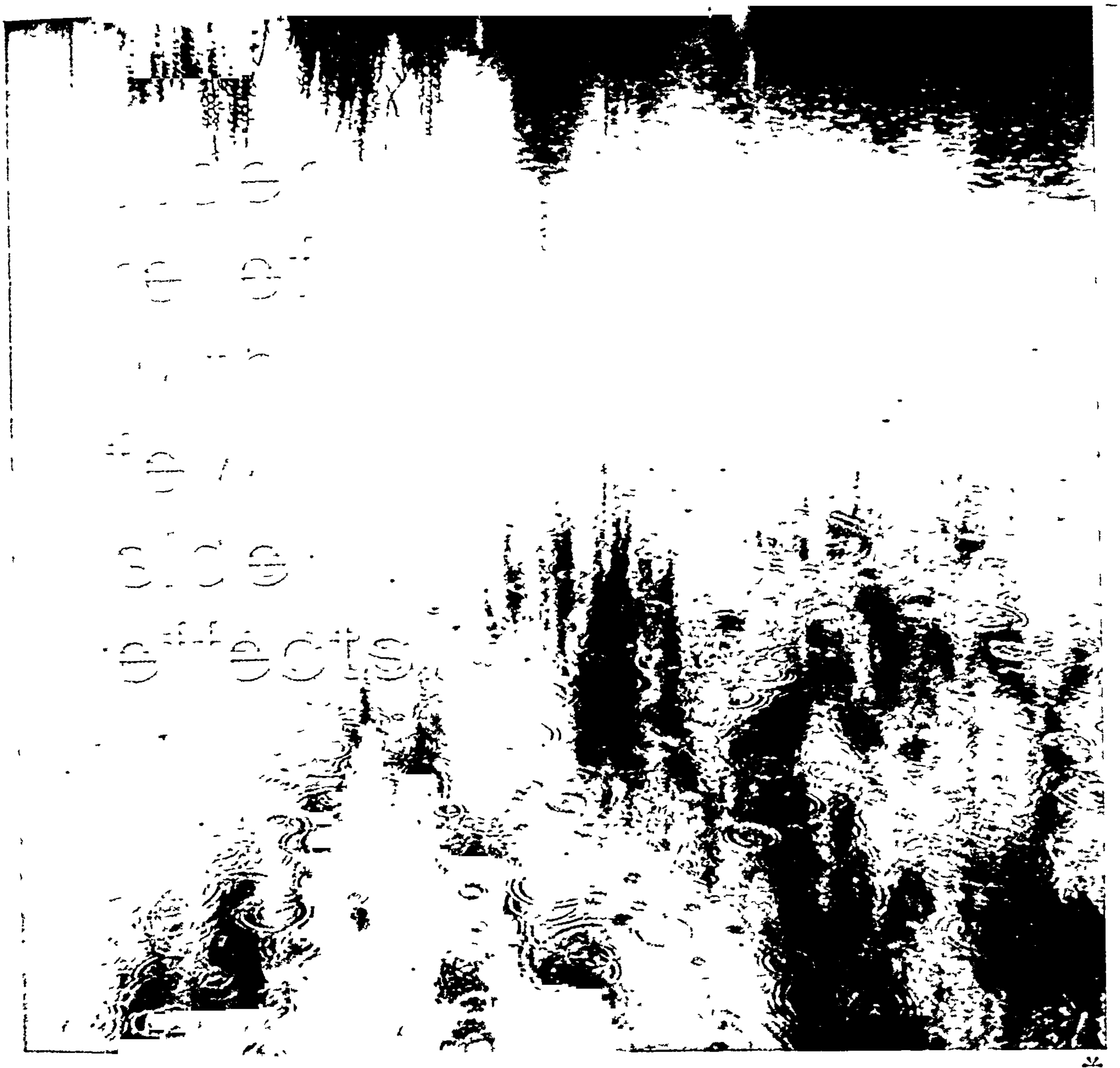
INTERNSHIP & RESIDENCY NUMBER: September 22, 1956

CLINICAL MEETING: October 20, 1956



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1 *Evaluation of Drugs in the Treatment of Peptic Ulcer* by J M Ruffin, M.D; D Cayer, M D, J S Atwater, M D, and B G Oren, M D Exhibit at A.M A. Meeting, Atlantic City, June, 1955

2 Council on Pharmacy and Chemistry *J A M A.* 160 389 (Feb 4) 1956

3 Council on Pharmacy and Chemistry *ibid*

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TONICS AND SEDATIVES

♣

my favorite story

In this space will be published anecdotes submitted by physicians concerning their practice or people in general. Contributions for "My Favorite Story" are welcome.

Jones had just made a killing on the stock market and now associated with new friends on a French luxury liner.

He wanted to show them how smart he was by ordering dessert from the foreign language menu. The waiter who took the order was astounded but went to fill his request and came back with a whole roast pig with an apple in its mouth.

Jones snatched the fruit from the pig's teeth.

"You know," he said smiling to his friends. "It's a funny thing, but this is the only way I like apples."

♣

the poetry corner

"The Typiste's Holiday"

My tYpust is io hor vacution,
My ripist's away fo r a week,
My tripudt us in hwr vacarion,
Wgile thse damn kews ploy hudge and seek.

Chorus:
Oh, brend bask, bting bzek,
Brung beej my blnnie ti ms, tp mr;
B)&ng llsj, b6iex,
Pping bozk m% beinino-o-ms CH% helk?

♣

♣

how it started

"Not worth a rap" does not refer to knocking the knuckles. In the language of a few hundred years ago it meant literally a thing of no value, for the allusion is to an 18th century Irish coin called a rap, worth about half a farthing, the equivalent of a quarter of an American cent.

♣

The "Roman salute," invented by D'Annunzio, which became also the German salute, was copied from some statue or fresco. He forgot that in ancient Rome citizens greeted each other by shaking hands. Only slaves made the sign adopted by the subjects of Mussolini and Hitler.

(Continued on page 74)

PHOSPHO-SODA (Fleet)
gentle...
prompt...
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A modern laxative of choice...
as evidenced by recent and continuing clinical evaluation.

A proven laxative...
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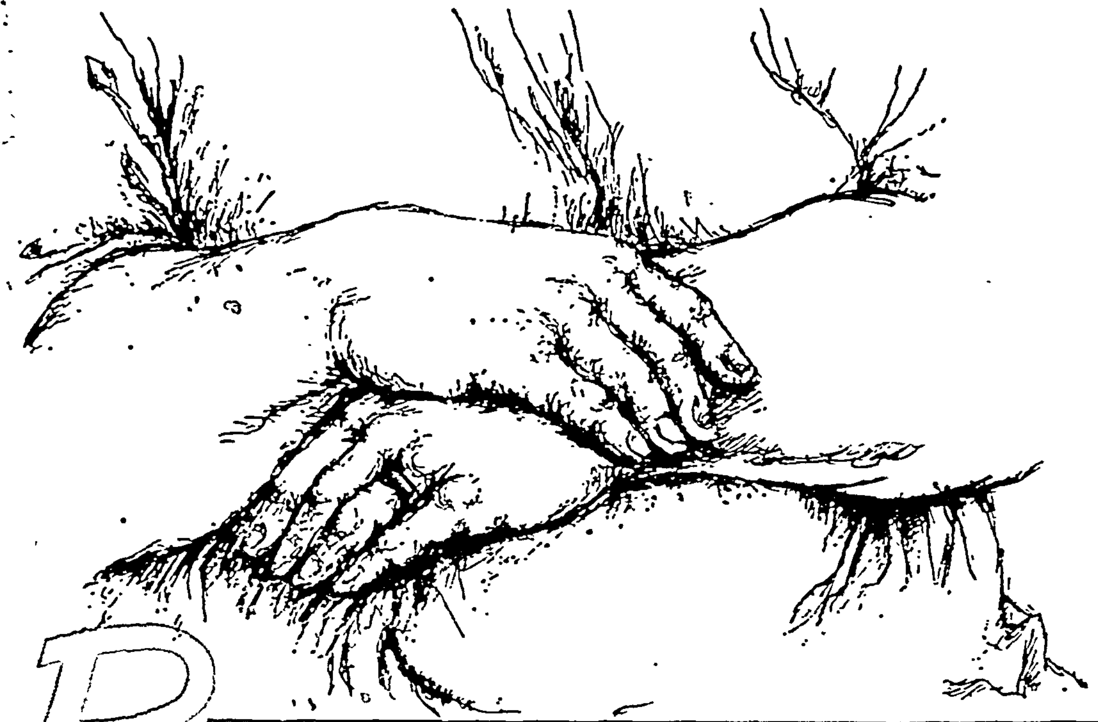
Doctor—it's up to you

to treat Obesity as a serious medical problem



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JAMA 1-12-57

TONICS AND SEDATIVES *(Continued)*

Among the ancient Greeks there was a class of men who learned how to make themselves welcome at the tables of rich men by providing dinner entertainment of a flattering nature.

To such men was applied the term "parasitos," made up from the prepositions "para" meaning beside and "sitos" meaning food.

The term was translated into the Latin as parasitus and into English as parasite.

◆

"Caesarean operation" has no relation to the birth of Julius Caesar. The term goes far into antiquity, and the operation is supposed to have been performed by early Greeks. The word "caesarean" derives from the Latin past participle "caesus" from "caedere" meaning to cut.

◆

quotes of the week

A young man went to see a lawyer but told him there would be no fee paid unless the lawyer felt sure there were grounds for legal action.

Then he gave the lawyer a detailed account of the trouble.

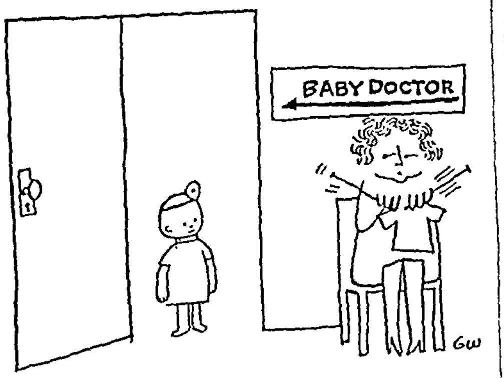
"Good Lord, the case is airtight!" shouted the lawyer. "The other fellow hasn't a leg to stand on. My advice is $50, and for an additional $100 retainer I will start suit."

"No," said the young man. "You'd better not."

"But why?" demanded the lawyer.

"Because I gave you the other fellow's side."

◆



◆

Smith used to play cards with the boys every Thursday. Then he got married.

Three weeks later he showed up again. The boys were naturally curious about his wedded bliss.

"Does she feed you well?" they asked.

"She gave me chicken three times last week and three times this week," Smith said proudly.

"Then you've no cause to complain?"

Smith's face dropped.

"Yes, I do," he said. "It was the same chicken."

◆

"Speeches are like babies—easy to conceive and hard to deliver."

(Continued on page 76)

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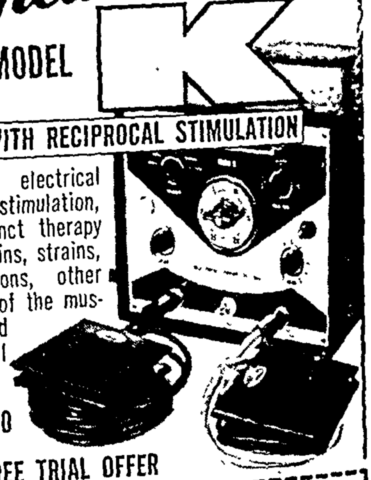
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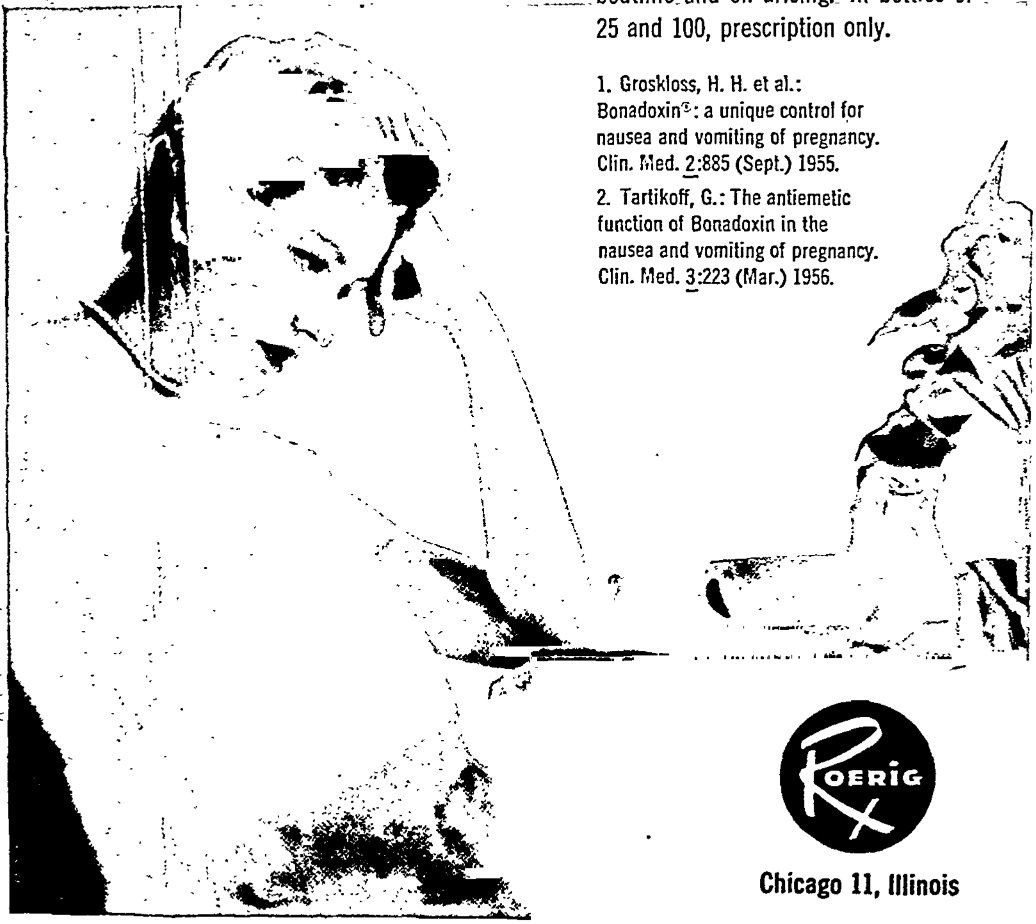
Mild cases: One BONADOXIN tablet at bedtime. Severe cases: One at bedtime and on arising. In bottles of 25 and 100, prescription only.

1. Groskloss, H. H. et al.: Bonadoxin®: a unique control for nausea and vomiting of pregnancy. Clin. Med. 2:885 (Sept.) 1955.
2. Tartikoff, G.: The antiemetic function of Bonadoxin in the nausea and vomiting of pregnancy. Clin. Med. 3:223 (Mar.) 1956.



ROERIG

Chicago 11, Illinois

TONICS AND SEDATIVES *(Continued)*

The gambler was delivering a monologue:

"For three nights straight I dreamed about salami, bolony, and liverwurst. Is that a hunch, or isn't it? I go to the track and in one race three horses by the names of Salami, Bolony, and Liverwurst are running. So I bet all three to win."

At this point a friend interrupted. "Which horse won?"

"A long shot by the name of Cold Cuts."

♣

A man walked into a restaurant, ordered a cup of coffee, and then proceeded to put 20 heaping spoonfuls of sugar in the cup. Then he sipped daintily at the contents.

"Why don't you stir it?" the restaurant owner asked angrily.

"Why should I? I don't like it sweet."

♣

She was one of the new rich, and she didn't hesitate about letting her friends know.

One day she got a jeweled wrist watch, and when one of the girls asked her the time, she said: "It's exactly two emeralds past the diamond."

♣

"To be positive is to be mistaken at the top of your voice."

♣

"It's a great kindness to trust people with a secret. They feel so important while telling it."

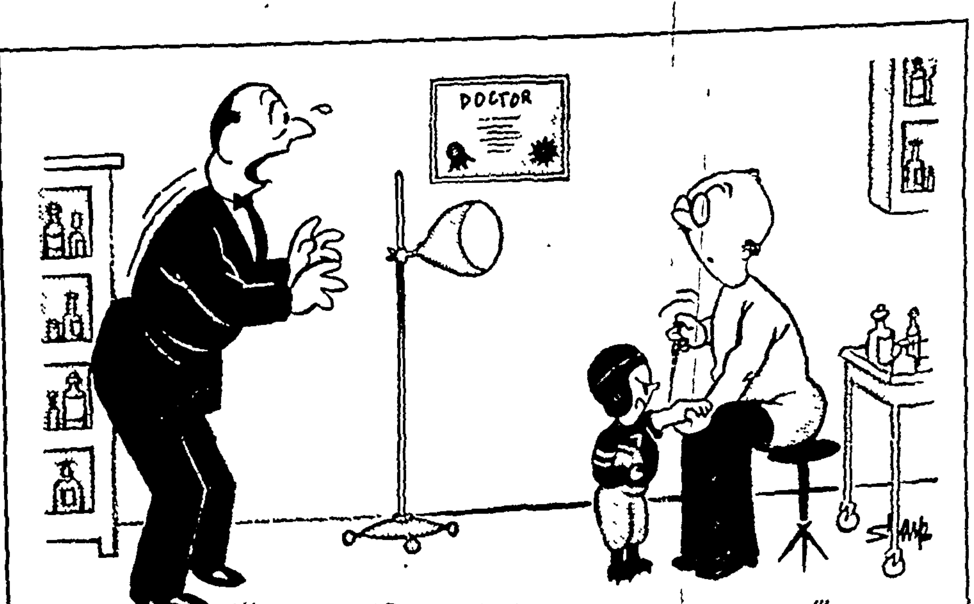
♣

"A smoothly running engine makes little noise and yet produces great power."

♣

"Facts are stubborn, but statistics are more pliable."

—D. D.



"Not in his left hand, doctor—that's his forward passing arm!"

Dr. Robert [illegible]
[illegible] Medical Coll[illegible]

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a clinically accepted method of menstrual hygiene

WESTERN JOURNAL OF SURGERY, OBSTETRICS

"Free from harm or irritation to the vaginal and cervical mucosa."
Karnaky, K. J.: Western Journal of Surgery, Obstetrics and Gynecology, Vol. 51, pp. 150-152.

AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY

"No evidence that the use of the tampon caused obstruction to menstrual flow."
Thornton, M. J.: American Journal of Obstetrics and Gynecology, Vol. 46, pp. 259-265.

THE JOURNAL

"Does not impair standard anatomic virginity."
Dickinson, R. L.: The Journal of the American Medical Association, Vol. 128, pp. 490-494.

Clinical Medicine

"Easy and comfortable to use and eliminated odor."
Sackren, H. S.: Clinical Medicine, Vol. 46, pp. 327-329.

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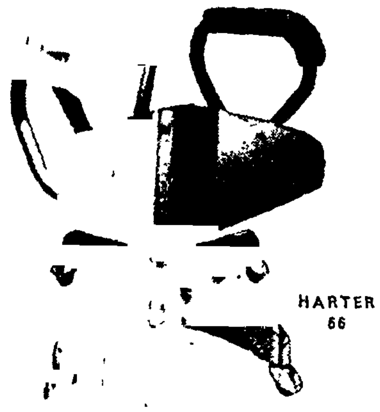

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